			the invention (including	and hematonoietic disorders
			antihodies and agonists or	(e \sigma as described below under
			anticodice and agomeses of	(c.g., as assembed solow and a
			antagonists of the invention) to	"Immune Activity", and
			regulate viability and	"Blood-Related Disorders"),
			proliferation of eosinophil cells	autoimmune diseases (e.g.,
			and cell lines. For example,	rheumatoid arthritis, systemic
			the CellTiter-Gloô	lupus erythematosis, Crohn"s
			Luminescent Cell Viability	disease, multiple sclerosis
			Assay (Promega Corp.,	and/or as described below),
			Madison, WI, USA) can be	immunodeficiencies (e.g., as
			used to measure the number of	described below). Highly
			viable cells in culture based on	preferred indications also
			quantitation of the ATP	include boosting or inhibiting
			present which signals the	immune cell proliferation.
			presence of metabolically	Preferred indications include
			active cells. Eosinophils are a	neoplastic diseases (e.g.,
			type of immune cell important	leukemia, lymphoma, and/or as
			in allergic responses; they are	described below under
			recruited to tissues and	"Hyperproliferative
			mediate the inflammtory	Disorders"). Highly preferred
			response of late stage allergic	indications include boosting an
			reaction. Eosinophil cell lines	eosinophil-mediated immune
			that may be used according to	response, and suppressing an
			these assays are publicly	eosinophil-mediated immune
			available and/or may be	response.
			routinely generated.	
			Exemplary eosinophil cells	
			that may be used according to	
			these assays include EOL-1	
			Cells.	
НЪРВQ71	1053	Production of	IFNgamma FMAT. IFNg plays	A highly preferred

embodiment of the invention	e includes a method for	stimulating the production of	IFNg. An alternative highly	preferred embodiment of the	invention includes a method	for inhibiting the production of	IFNg. Highly preferred	indications include blood	y   disorders (e.g., as described	below under "Immune	Activity", "Blood-Related	Disorders", and/or	"Cardiovascular Disorders"),	and infection (e.g., viral	infections, tuberculosis,		chronic granulomatosus	disease and malignant	osteoporosis, and/or as	described below under	winfectious Disease"). Highly	preferred indications include	autoimmune disease (e.g.,	rheumatoid arthritis, systemic	lupus erythematosis, multiple	sclerosis and/or as described	below), immunodeficiency	(e.g., as described below),	boosting a T cell-mediated	immine reconce and
a central role in the immune	system and is considered to be	a proinflammatory cytokine.	IFNg promotes TH1 and	inhibits TH2 differentiation;	promotes IgG2a and inhibits	IgE secretion; induces	macrophage activation; and	increases MHC expression.	Assays for immunomodulatory	proteins produced by T cells	and NK cells that regulate a	variety of inflammatory	activities and inhibit TH2	helper cell functions are well	known in the art and may be	used or routinely modified to	assess the ability of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) to mediate	immunomodulation, regulate	inflammatory activities,	modulate TH2 helper cell	function, and/or mediate	humoral or cell-mediated	immunity. Exemplary assays	that test for	immunomodulatory proteins	evaluate the production of
IFNgamma using a	T cells																													
105																														

	cytokines, such as Interferon	suppressing a T cell-mediated
 	gamma (IFNg), and the	immune response. Additional
	activation of T cells. Such	highly preferred indications
	assays that may be used or	include inflammation and
	routinely modified to test	inflammatory disorders.
	immunomodulatory activity of	Additional preferred
	polypeptides of the invention	indications include idiopathic
	(including antibodies and	pulmonary fibrosis. Highly
	agonists or antagonists of the	preferred indications include
	invention) include the assays	neoplastic diseases (e.g.,
	disclosed in Miraglia et al., J	leukemia, lymphoma,
 	Biomolecular Screening 4:193-	melanoma, and/or as described
	204 (1999); Rowland et al.,	below under
	"Lymphocytes: a practical	"Hyperproliferative
	approach" Chapter 6:138-160	Disorders"). Highly preferred
	(2000); Gonzalez et al., J Clin	indications include neoplasms
	Lab Anal 8(5):225-233 (1995);	and cancers, such as, for
 -	Billiau et al., Ann NY Acad	example, leukemia, lymphoma,
	Sci 856:22-32 (1998); Boehm	melanoma, and prostate,
	et al., Annu Rev Immunol	breast, lung, colon, pancreatic,
	15:749-795 (1997), and	esophageal, stomach, brain,
 	Rheumatology (Oxford)	liver and urinary cancer. Other
	38(3):214-20 (1999), the	preferred indications include
	contents of each of which are	benign dysproliferative
	herein incorporated by	disorders and pre-neoplastic
 	reference in its entirety.	conditions, such as, for
	Human T cells that may be	example, hyperplasia,
	used according to these assays	metaplasia, and/or dysplasia.
 	may be isolated using	Preferred indications include
	techniques disclosed herein or	anemia, pancytopenia,
	otherwise known in the art.	leukopenia, thrombocytopenia,

				Human T cells are primary human lymphocytes that mature in the thymus and express a T Cell receptor and CD3, CD4, or CD8. These cells mediate humoral or cellmediated immunity and may be preactivated to enhance responsiveness to immunomodulatory factors.	Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, asthma and allergy.
106	HDPCJ91	1054	Activation of Skeletal Mucle Cell PI3 Kinase Signalling Pathway	Kinase assay. Kinase assays, for example an GSK-3 kinase assay, for PI3 kinase signal transduction that regulate glucose metabolism and cell survivial are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote or inhibit glucose metabolism and cell survival. Exemplary assays for PI3 kinase activity that may be	A highly preferred embodiment of the invention includes a method for increasing muscle cell survival An alternative highly preferred embodiment of the invention includes a method for decreasing muscle cell survival. A preferred embodiment of the invention includes a method for stimulating muscle cell proliferation. In a specific embodiment, skeletal muscle cell proliferation is stimulated. An alternative highly preferred

used or routinely modified to test PI3 kinase-induced activity	embodiment of the invention includes a method for
or polypeptides or the invention (including antibodies	innibiting muscle cell proliferation. In a specific
and agonists or antagonists of	embodiment, skeletal muscle
the invention) include assays disclosed in Forrer et al., Biol	cell proliteration is inhibited.  A preferred embodiment of
Chem 379(8-9):1101-1110	the invention includes a
 (1998); Nikoulina et al.,	method for stimulating muscle
 Diabetes 49(2):263-271	cell differentiation. In a
 (2000); and Schreyer et al.,	specific embodiment, skeletal
   Diabetes 48(8):1662-1666	muscle cell differentiation is
(1999), the contents of each of	stimulated. An alternative
which are herein incorporated	highly preferred embodiment
by reference in its entirety.	of the invention includes a
 Rat myoblast cells that may be	method for inhibiting muscle
 used according to these assays	cell differentiation. In a
are publicly available (e.g.,	specific embodiment, skeletal
 through the ATCC).	muscle cell differentiation is
Exemplary rat myoblast cells	inhibited. Highly preferred
that may be used according to	indications include disorders of
 these assays include L6 cells.	the musculoskeletal system.
L6 is an adherent rat myoblast	Preferred indications include
 cell line, isolated from primary	neoplastic diseases (e.g., as
 cultures of rat thigh muscle,	described below under
that fuses to form	"Hyperproliferative
 multinucleated myotubes and	Disorders"), endocrine
 striated fibers after culture in	disorders (e.g., as described
 differentiation media.	below under "Endocrine
	Disorders"), neural disorders
	(e.g., as described below under

blockage), seizures, mental	confusion, drowsiness,	nonketotic hyperglycemic-	hyperosmolar coma,	cardiovascular disease (e.g.,	heart disease, atherosclerosis,	microvascular disease,	hypertension, stroke, and other	diseases and disorders as	described in the	"Cardiovascular Disorders"	section below), dyslipidemia,	endocrine disorders (as	described in the "Endocrine	Disorders" section below),	neuropathy, vision impairment	(e.g., diabetic retinopathy and	blindness), ulcers and impaired	wound healing, infections	(e.g., infectious diseases and	disorders as described in the	"Infectious Diseases" section	below, especially of the	urinary tract and skin), carpal	tunnel syndrome and	Dupuytren's contracture).	An additional highly preferred	indication is obesity and/or	complications associated with	obesity. Additional highly	preferred indications include
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																												_		

weight loss or alternatively, weight gain. Additional	highly preferred indications are complications associated with	Additional highly preferred	indications are disorders of the musculoskeletal system	including myopathies,	muscular dystrophy, and/or as described herein.	Additional highly preferred	indications include: myopathy,	failure, cachexia, myxomas,	fibromas, congenital	cardiovascular abnormalities,	heart disease, cardiac arrest,	heart valve disease, and vascular disease. Highly	ons	neoplasms and cancer, such as,	rhabdomyoma,	rhabdosarcoma, stomach,	esophageal, prostate, and	urinary cancer. Preferred	indications also include breast,	lung, colon, pancreatic, brain,	and liver cancer. Other	preferred indications include
																					-	

					disorders and pre-neoplastic
					conditions, such as, hyperplasia, metaplasia, and/or
					dysplasia.
	HDPC025	1055	Regulation of	Assays for the regulation of	A highly preferred indication
107			viability and	viability and proliferation of	is diabetes mellitus. An
	7.		proliferation of	cells in vitro are well-known in	additional highly preferred
<del></del>			pancreatic beta	the art and may be used or	indication is a complication
			cells.	routinely modified to assess	associated with diabetes (e.g.,
			,	the ability of polypeptides of	diabetic retinopathy, diabetic
				the invention (including	nephropathy, kidney disease
				antibodies and agonists or	(e.g., renal failure,
				antagonists of the invention) to	nephropathy and/or other
				regulate viability and	diseases and disorders as
				proliferation of pancreatic beta	described in the "Renal
				cells. For example, the Cell	Disorders" section below),
				Titer-Glo luminescent cell	diabetic neuropathy, nerve
				viability assay measures the	disease and nerve damage
				number of viable cells in	(e.g., due to diabetic
	<u>-</u>		í	culture based on quantitation	neuropathy), blood vessel
				of the ATP present which	blockage, heart disease, stroke,
				signals the presence of	impotence (e.g., due to diabetic
				metabolically active cells.	neuropathy or blood vessel
				Exemplary assays that may be	blockage), seizures, mental
				used or routinely modified to	confusion, drowsiness,
				test regulation of viability and	nonketotic hyperglycemic-
				proliferation of pancreatic beta	hyperosmolar coma,
				cells by polypeptides of the	cardiovascular disease (e.g.,
				invention (including antibodies	heart disease, atherosclerosis,
				and agonists or antagonists of	microvascular disease,
				the invention) include assays	hypertension, stroke, and other

diseases and disorders as described in the "Cardiovascular Disorders" section below), dyslipidemia, endocrine disorders (as	described in the "Endocrine Disorders" section below), neuropathy, vision impairment (e.g., diabetic retinopathy and blindness), ulcers and impaired wound healing, and infection (e.g., infectious diseases and	disorders as described in the "Infectious Diseases" section below, especially of the urinary tract and skin), carpal tunnel syndrome and Dupuytren's contracture). An additional highly preferred indication is obesity and/or	complications associated with obesity. Additional highly preferred indications include weight loss or alternatively, weight gain. Additional highly preferred indications are complications associated with insulin resistance.
disclosed in: Ohtani KI, et al., Endocrinology, 139(1):172-8 (1998); Krautheim A, et al, Exp Clin Endocrinol Diabetes, 107 (1):29-34 (1999), the	contents of each of which is herein incorporated by reference in its entirety. Pancreatic cells that may be used according to these assays are publicly available (e.g., through the ATCC) and/or	may be routinely generated. Exemplary pancreatic cells that may be used according to these assays include HITT15 Cells. HITT15 are an adherent epithelial cell line established from Syrian hamster islet cells transformed with SV40. These	cells express glucagon, somatostatin, and glucocorticoid receptors. The cells secrete insulin, which is stimulated by glucose and glucagon and suppressed by somatostatin or glucocorticoids. ATTC# CRL-1777 Refs: Lord and Ashcroft. Biochem. J. 219: 547-551; Santerre et al. Proc.

				Natl. Acad. Sci. USA 78:	
				4339-4343, 1981.	
	HDPC025	1055	Activation of	Assays for the activation of	Highly preferred indications
107			transcription	transcription through the	include inflammation and
	·		through NFKB	NFKB response element are	inflammatory disorders.
			response element in	well-known in the art and may	Highly preferred indications
			immune cells (such	be used or routinely modified	include blood disorders (e.g.,
	-		as T-cells).	to assess the ability of	as described below under
		,		polypeptides of the invention	"Immune Activity", "Blood-
· -				(including antibodies and	Related Disorders", and/or
				agonists or antagonists of the	"Cardiovascular Disorders").
				invention) to regulate NFKB	Highly preferred indications
				transcription factors and	include autoimmune diseases
				modulate expression of	(e.g., rheumatoid arthritis,
				immunomodulatory genes.	systemic lupus erythematosis,
				Exemplary assays for	multiple sclerosis and/or as
				transcription through the	described below), and
-4-2				NFKB response element that	immunodeficiencies (e.g., as
				may be used or rountinely	described below). An
				modified to test NFKB-	additional highly preferred
				response element activity of	indication is infection (e.g.,
-				polypeptides of the invention	AIDS, and/or an infectious
				(including antibodies and	disease as described below
				agonists or antagonists of the	under "Infectious Disease").
				invention) include assays	Highly preferred indications
-10				disclosed in Berger et al., Gene	include neoplastic diseases
				66:1-10 (1998); Cullen and	(e.g., melanoma, leukemia,
	1.			Malm, Methods in Enzymol	lymphoma, and/or as described
				216:362-368 (1992); Henthorn	below under
				et al., Proc Natl Acad Sci USA	"Hyperproliferative
				85:6342-6346 (1988); Black et	Disorders"). Highly preferred

		al Virus Gnes 15(2):105-117	indications include neoplasms
		(1997): and Fraser et al	and cancers, such
-		29(3):838-844 (1999), the	as,melanoma, renal cell
		contents of each of which are	carcinoma, leukemia,
	•	herein incorporated by	lymphoma, and prostate,
		reference in its entirety. T	breast, lung, colon, pancreatic,
		cells that may be used	esophageal, stomach, brain,
		according to these assays are	liver and urinary cancer. Other
		publicly available (e.g.,	preferred indications include
		through the ATCC).	benign dysproliferative
		Exemplary human T cells that	disorders and pre-neoplastic
		may be used according to these	conditions, such as, for
		assays include the SUPT cell	example, hyperplasia,
		line, which is a suspension	metaplasia, and/or dysplasia.
		culture of IL-2 and IL-4	Preferred indications also
		responsive T cells.	include anemia, pancytopenia,
		 1	leukopenia, thrombocytopenia,
			Hodgkin's disease, acute
			lymphocytic anemia (ALL),
			plasmacytomas, multiple
			myeloma, Burkitt's lymphoma,
			arthritis, AIDS,
			granulomatous disease,
			inflammatory bowel disease,
			sepsis, neutropenia,
			neutrophilia, psoriasis,
			hemophilia, hypercoagulation,
			diabetes mellitus, endocarditis,
			meningitis, Lyme Disease,
			suppression of immune
			reactions to transplanted

					organs, asthma and allergy.
	HDPCY37	1056	Activation of	Assays for the activation of	A highly preferred indication
108			transcription	transcription through the	is obesity and/or complications
			through cAMP	cAMP response element are	associated with obesity.
		•	response element	well-known in the art and may	Additional highly preferred
· ·			(CRE) in pre-	be used or routinely modified	indications include weight loss
			adipocytes.	to assess the ability of	or alternatively, weight gain.
				polypeptides of the invention	An additional highly preferred
۸				(including antibodies and	indication is diabetes mellitus.
				agonists or antagonists of the	An additional highly preferred
				invention) to increase cAMP,	indication is a complication
				regulate CREB transcription	associated with diabetes (e.g.,
				factors, and modulate	diabetic retinopathy, diabetic
				expression of genes involved	nephropathy, kidney disease
				in a wide variety of cell	(e.g., renal failure,
				functions. For example, a	nephropathy and/or other
				3T3-L1/CRE reporter assay	diseases and disorders as
				may be used to identify factors	described in the "Renal
				that activate the cAMP	Disorders" section below),
				signaling pathway. CREB	diabetic neuropathy, nerve
				plays a major role in	disease and nerve damage
<del>1</del>	<del>-</del>			adipogenesis, and is involved	(e.g., due to diabetic
				in differentiation into	neuropathy), blood vessel
				adipocytes. CRE contains the	blockage, heart disease, stroke,
				binding sequence for the	impotence (e.g., due to diabetic
				transcription factor CREB	neuropathy or blood vessel
				(CRE binding protein).	blockage), seizures, mental
				Exemplary assays for	confusion, drowsiness,
				transcription through the	nonketotic hyperglycemic-
				cAMP response element that	hyperosmolar coma,
				may be used or routinely	cardiovascular disease (e.g.,

 		modified to test cAMP-	heart disease, atherosclerosis,
 		response element activity of	microvascular disease,
		polypeptides of the invention	hypertension, stroke, and other
	-	(including antibodies and	diseases and disorders as
		agonists or antagonists of the	described in the
		invention) include assays	"Cardiovascular Disorders"
 		disclosed in Berger et al., Gene	section below), dyslipidemia,
		66:1-10 (1998); Cullen and	endocrine disorders (as
		Malm, Methods in Enzymol	described in the "Endocrine
 		216:362-368 (1992); Henthorn	Disorders" section below),
 		et al., Proc Natl Acad Sci USA	neuropathy, vision impairment
		85:6342-6346 (1988); Reusch	(e.g., diabetic retinopathy and
 		et al., Mol Cell Biol	blindness), ulcers and impaired
		20(3):1008-1020 (2000); and	wound healing, and infection
 		Klemm et al., J Biol Chem	(e.g., infectious diseases and
		273:917-923 (1998), the	disorders as described in the
 		contents of each of which are	"Infectious Diseases" section
		herein incorporated by	below, especially of the
 		reference in its entirety. Pre-	urinary tract and skin), carpal
		adipocytes that may be used	tunnel syndrome and
		according to these assays are	Dupuytren's contracture).
		publicly available (e.g.,	Additional highly preferred
		through the ATCC) and/or	indications are complications
		may be routinely generated.	associated with insulin
		Exemplary mouse adipocyte	resistance.
		cells that may be used	
 		according to these assays	
		include 3T3-L1 cells. 3T3-L1	
		is an adherent mouse	
 		preadipocyte cell line that is a	
		continuous substrain of 3T3	

HDPCY37 108 HDPCY37 108	1056	SEAP in OE-33 Activation of transcription through NFKB response element in immune cells (such	undergo a pre-adipocyte to adipose-like conversion under appropriate differentiation conditions known in the art.  Assays for the activation of transcription through the	
	1056	3 nt in such	appropriate differentiation conditions known in the art. Assays for the activation of transcription through the	
	1056	3 nt in such	conditions known in the art. Assays for the activation of transcription through the	
	1056	SEAP in OE-33 Activation of transcription through NFKB response element in immune cells (such	Assays for the activation of transcription through the	
	1056	Activation of transcription through NFKB response element in immune cells (such	Assays for the activation of transcription through the	
108		transcription through NFKB response element in immune cells (such	transcription through the	Highly preferred indications
		through NFKB response element in immune cells (such		include inflammation and
		response element in immune cells (such	NFKB response element are	inflammatory disorders.
		immune cells (such	well-known in the art and may	Highly preferred indications
		,	be used or routinely modified	include blood disorders (e.g.,
		as T-cells).	to assess the ability of	as described below under
			polypeptides of the invention	"Immune Activity", "Blood-
			(including antibodies and	Related Disorders", and/or
			agonists or antagonists of the	"Cardiovascular Disorders").
			invention) to regulate NFKB	Highly preferred indications
			transcription factors and	include autoimmune diseases
			modulate expression of	(e.g., rheumatoid arthritis,
			immunomodulatory genes.	systemic lupus erythematosis,
			Exemplary assays for	multiple sclerosis and/or as
			transcription through the	described below), and
			NFKB response element that	immunodeficiencies (e.g., as
			may be used or rountinely	described below). An
			modified to test NFKB-	additional highly preferred
			response element activity of	indication is infection (e.g.,
			polypeptides of the invention	AIDS, and/or an infectious
			(including antibodies and	disease as described below
			agonists or antagonists of the	under "Infectious Disease").
			invention) include assays	Highly preferred indications

include neoplastic diseases (e.g., melanoma, leukemia,	lymphoma, and/or as described	below under	"Hyperproliferative	Disorders"). Highly preferred	indications include neoplasms	and cancers, such	as,melanoma, renal cell	carcinoma, leukemia,	lymphoma, and prostate,	breast, lung, colon, pancreatic,	esophageal, stomach, brain,	liver and urinary cancer. Other	preferred indications include	benign dysproliferative	disorders and pre-neoplastic	conditions, such as, for	example, hyperplasia,	metaplasia, and/or dysplasia.	Preferred indications also	include anemia, pancytopenia,	leukopenia, thrombocytopenia,	Hodgkin's disease, acute	lymphocytic anemia (ALL),	plasmacytomas, multiple	myeloma, Burkitt's lymphoma,	arthritis, AIDS,	granulomatous disease,	inflammatory bowel disease,	sepsis, neutropenia,
disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and	Malm, Methods in Enzymol	216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA	85:6342-6346 (1988); Black et	al., Virus Gnes 15(2):105-117	(1997); and Fraser et al.,	29(3):838-844 (1999), the	contents of each of which are	herein incorporated by	reference in its entirety. T	cells that may be used	according to these assays are	publicly available (e.g.,	through the ATCC).	Exemplary human T cells that	may be used according to these	assays include the SUPT cell	line, which is a suspension	culture of IL-2 and IL-4	responsive T cells.									
		-																								-			
																											-		

					neutrophilia, psoriasis, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningits I vme Disease
					suppression of immune
					organs, asthma and allergy.
000	HDPCY37	1056	Production of IL-10	Assays for production of IL-10	Highly preferred indications
108			and activation of 1-cells.	and activation of 1-cells are well known in the art and may	include allergy and astrima. Additional highly preferred
				be used or routinely modified	indications include immune
				to assess the ability of	and hematopoietic disorders
			),	polypeptides of the invention	(e.g., as described below under
				(including antibodies and	"Immune Activity", and
				agonists or antagonists of the	"Blood-Related Disorders"),
				invention) to stimulate or	autoimmune diseases (e.g.,
				inhibit production of IL-10	rheumatoid arthritis, systemic
				and/or activation of T-cells.	lupus erythematosis, Crohn"s
				Exemplary assays that may be	disease, multiple sclerosis
				used or routinely modified to	and/or as described below),
		-		assess the ability of	immunodeficiencies (e.g., as
				polypeptides and antibodies of	described below), boosting a T
				the invention (including	cell-mediated immune
				agonists or antagonists of the	response, and suppressing a T
				invention) to modulate IL-10	cell-mediated immune
		~		production and/or T-cell	response.
				proliferation include, for	
				example, assays such as	
				disclosed and/or cited in:	
				Robinson, DS, et al., "Th-2	
				cytokines in allergic disease"	

				helper type 2 cell-directed therapy for asthma" Pharmacology & Therapeutics; 88: 187-196 (2000); the contents of each of which are herein incorporated by reference in their entirety. Exemplary cells that may be used according to these assays include Th2 cells. IL10 secreted from Th2 cells may be measured as a marker of Th2 cell activation. Th2 cells are a class of T cells that secrete IL4, IL10, IL13, IL5 and IL6. Factors that induce differentiation and activation of Th2 cells play a major role in the initiation and pathogenesis of allergy and asthma. Primary T helper 2 cells are generated via in vitro	
				culture under 1 nz polarizing conditions using peripheral blood lymphocytes isolated from cord blood	
109	HDPFB02	1057	SEAP in HIB/CRE		
	HDPFB02	1057	Activation of	This reporter assay measures	Highly preferred indications

		66.1 10 (1000). Cullen and	Disordana" Other wasterned
		00.1-10 (1970), Cuitan and	Disorders ): Other profession
		Malm, Methods in Enzymol	indications include benign
		216:362-368 (1992); Henthorn	dysproliferative disorders and
		et al., Proc Natl Acad Sci USA	pre-neoplastic conditions, such
		85:6342-6346 (1988); Flavell	as, for example, hyperplasia,
		et al., Cold Spring Harb Symp	metaplasia, and/or dysplasia.
		Quant Biol 64:563-571 (1999);	Preferred indications include
		Rodriguez-Palmero et al., Eur	anemia, pancytopenia,
		J Immunol 29(12):3914-3924	leukopenia, thrombocytopenia,
		(1999); Zheng and Flavell,	leukemias, Hodgkin's disease,
		Cell 89(4):587-596 (1997); and	acute lymphocytic anemia
		Henderson et al., Mol Cell Biol	(ALL), plasmacytomas,
		14(6):4286-4294 (1994), the	multiple myeloma, Burkitt's
		contents of each of which are	lymphoma, arthritis, AIDS,
		herein incorporated by	granulomatous disease,
		reference in its entirety. Mast	inflammatory bowel disease,
		cells that may be used	sepsis, neutropenia,
		according to these assays are	neutrophilia, psoriasis,
		publicly available (e.g.,	suppression of immune
		through the ATCC).	reactions to transplanted
		Exemplary human mast cells	organs and tissues, hemophilia,
		that may be used according to	hypercoagulation, diabetes
		these assays include the HMC-	mellitus, endocarditis,
		1 cell line, which is an	meningitis, and Lyme Disease.
		immature human mast cell line	
		established from the peripheral	
		blood of a patient with mast	
		cell leukemia, and exhibits	
		many characteristics of	
		immature mast cells.	
HDPFB02 1057	Production of	Endothelial cells, which are	Highly preferred indications

109		ICAM in	cells that line blood vessels,	include inflammation (acute
		endothelial cells	and are involved in functions	and chronic), restnosis,
		(such as human	that include, but are not limited	atherosclerosis, asthma and
		umbilical vein	to, angiogenesis, vascular	allergy. Highly preferred
		 endothelial cells	permeability, vascular tone,	indications include
		(HUVEC))	and immune cell extravasation.	inflammation and
			Exemplary endothelial cells	inflammatory disorders,
			that may be used in ICAM	immunological disorders,
			production assays include	neoplastic disorders (e.g.
			human umbilical vein	cancer/tumorigenesis), and
	*		endothelial cells (HUVEC),	cardiovascular disorders (such
			and are available from	as described below under
	, -		commercial sources. The	"Immune Activity", "Blood-
	-		expression of ICAM (CD54),a	Related Disorders",
		-	intergral membrane protein,	"Hyperproliferative Disorders"
			can be upregulated by	and/or "Cardiovascular
			cytokines or other factors, and	Disorders"). Highly preferred
			ICAM expression is important	indications include neoplasms
			in mediating immune and	and cancers such as, for
			endothelial cell interactions	example, leukemia, lymphoma,
		-	leading to immune and	melanoma, renal cell
			inflammatory responses.	carcinoma, and prostate,
			Assays for measuring	breast, lung, colon, pancreatic,
			expression of ICAM-1 are	esophageal, stomach, brain,
			well-known in the art and may	liver and urinary cancer. Other
			be used or routinely modified	preferred indications include
			to assess the ability of	benign dysproliferative
			polypeptides of the invention	disorders and pre-neoplastic
			(including antibodies and	conditions, such as, for
			agonists or antagonists of the	example, hyperplasia,
			invention) to regulate ICAM-1	metaplasia, and/or dysplasia.

HDPFF39	1058	Activation of T-Cell p38 or JNK	that may be used or routinely modified to measure ICAM-1 expression include assays disclosed in: Rolfe BE, et al., Atherosclerosis, 149(1):99-110 (2000); Panettieri RA Jr, et al., J Immunol, 154(5):2358-2365 (1995); and, Grunstein MM, et al., Am J Physiol Lung Cell Mol Physiol, 278(6):L1154-L1163 (2000), the contents of each of which is herein incorporated by reference in its entirety.  Kinase assay. JNK and p38 kinase assays for signal	Preferred indications include neoplastic diseases (e.g., as
		Signaling Pathway.	transduction that regulate cell proliferation, activation, or apoptosis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote or inhibit immune cell (e.g. T-cell) proliferation, activation, and apoptosis. Exemplary assays for JNK and p38 kinase activity that may be	described below under "Hyperproliferative Disorders"), blood disorders (e.g., as described below under "Immune Activity", "Cardiovascular Disorders", and/or "Blood-Related Disorders"), and infection (e.g., an infectious disease as described below under "Infectious Disease"). Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic

		used or routinely modified to	lunus erythematosis, multiple
		test JNK and n38 kinase-	sclerosis and/or as described
		induced activity of	below) and
-		polypeptides of the invention	immunodeficiencies (e.g., as
		(including antibodies and	described below). Additional
		agonists or antagonists of the	highly preferred indications
		invention) include the assays	include inflammation and
		disclosed in Forrer et al., Biol	inflammatory disorders.
		Chem 379(8-9):1101-1110	Highly preferred indications
		(1998); Gupta et al., Exp Cell	also include neoplastic
		Res 247(2): 495-504 (1999);	diseases (e.g., leukemia,
		Kyriakis JM, Biochem Soc	lymphoma, and/or as described
	-	Symp 64:29-48 (1999); Chang	below under
		and Karin, Nature	"Hyperproliferative
		410(6824):37-40 (2001); and	Disorders"). Highly preferred
		Cobb MH, Prog Biophys Mol	indications include neoplasms
		Biol 71(3-4):479-500 (1999);	and cancers, such as, leukemia,
		the contents of each of which	lymphoma, prostate, breast,
		are herein incorporated by	lung, colon, pancreatic,
		reference in its entirety. T	esophageal, stomach, brain,
		cells that may be used	liver, and urinary cancer. Other
		according to these assays are	preferred indications include
		publicly available (e.g.,	benign dysproliferative
		through the ATCC).	disorders and pre-neoplastic
		Exemplary mouse T cells that	conditions, such as, for
		may be used according to these	example, hyperplasia,
		assays include the CTLL cell	metaplasia, and/or dysplasia.
		line, which is an IL-2	Preferred indications include
		dependent suspension-culture	arthritis, asthma, AIDS,
		cell line with cytotoxic	allergy, anemia, pancytopenia,
		activity.	leukopenia, thrombocytopenia,

					Hodgkin"s disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt"s lymphoma, granulomatous disease, inflammatory bowel disease, sepsis, psoriasis, suppression of immune reactions to transplanted organs and tissues, endocarditis, meningitis, and Lyme Disease.
110	HDPFF39	1058	Inhibition of squalene synthetase gene transcription.	Reporter Assay: construct contains regulatory and coding sequence of squalene synthetase, the first specific enzyme in the cholesterol biosynthetic pathway. See Jiang, et al., J. Biol. Chem. 268:12818-128241(993), the contents of which are herein incorporated by reference in its entirety. Cells were treated with SID supernatants, and SEAP activity was measured after 72 hours. HepG2 is a human hepatocellular carcinoma cell line (ATCC HB-8065). See Knowles et al., Science. 209:497-9 (1980), the contents of which are herein incorporated by reference in its	

				entirety.	
	HDPFP29	1059	Myoblast cell	Assays for muscle cell	Highly preferred indications
111			proliferation	proliferation are well known in	include diabetes, myopathy,
		~		the art and may be used or	muscle cell atrophy, cancers of
		·		routinely modified to assess	muscle (such as,
				the ability of polypeptides of	rhabdomyoma, and
	-			the invention (including	rhabdosarcoma),
				antibodies and agonists or	cardiovascular disorders (such
				antagonists of the invention) to	as congestive heart failure,
				stimulate or inhibit myoblast	cachexia, myxomas, fibromas,
				cell proliferation. Exemplary	congenital cardiovascular
				assays for myoblast cell	abnormalities, heart disease,
				proliferation that may be used	cardiac arrest, heart valve
				or routinely modified to test	disease, vascular disease, and
				activity of polypeptides and	also as described below under
				antibodies of the invention	"Cardiovascular Disorders"),
				(including agonists or	stimulating myoblast
				antagonists of the invention)	proliferation, and inhibiting
			-	include, for example, assays	myoblast proliferation.
				disclosed in: Soeta, C., et al.	
				"Possible role for the c-ski	
				gene in the proliferation of	
				myogenic cells in regenerating	
				skeletal muscles of rats" Dev	
				Growth Differ Apr;43(2):155-	
				64 (2001); Ewton DZ, et al.,	
				"IGF binding proteins-4, -5	
				and -6 may play specialized	
				roles during L6 myoblast	
				proliferation and	
				differentiation" J Endocrinol	

that that hese slast corm and in und in und in und seell result.					Mar;144(3):539-53 (1995); and, Pampusch MS, et	
proliferation of L6 and embryonic porcine myogenic cells" J Cell Physiol Jun;143(3):524-8 (1990); the contents of each of which are herein incorporated by reference in their entirety. Exemplary myoblast cells that may be used according to these assays include the rat myoblast L6 cells are an adherent rat myoblast cell line, isolated from primary cultures of rat thigh muscle, that fuse to form multinucleated myotubes and striated fibers after culture in differentiation media  Basays. Include the rat myoblast L6 cells are an adherent rat myoblast Cell line, Rat myoblast L6 cells are an adherent rat myoblast Cell line, solated from primary cultures of rat thigh muscle, that fuse to form multinucleated fibers and striated fibers after culture in differentiation media  Basays include the rat myoblast L6 cells are an adherent rat myoblast Cell line, solated from primary cultures of rat thigh muscle, that fuse to form multinucleated fibers and striated fibers are culture in differentiation media  Endothelial Cell kinase assays for signal pagnosis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including					al.," Effect of transforming growth factor beta on	
embryonic porcine myogenic cells" J Cell Physiol Jun;143(3):524-8 (1990); the contents of each of which are herein incorporated by reference in their entirety. Exemplary myoblast cells that may be used according to these assays include the rat myoblast L6 cells are an adherent rat myoblast cells are an adherent rat myoblast cell line. Rat myoblast L6 cells are an adherent rat myoblast cell line, isolated from primary cultures of rat thigh muscle, that fuse to form multinucleated myotubes and striated fibers after culture in differentiation media.  HDPG149 1060 Activation of Kinase assay. JNK and p38 Endothelial Cell kinase assays. JNK and p38 Endothelial Cell kinase assays for signal ransduction that regulate cell Signaling Pathway. proliferation, activation, or apoptosis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including					proliferation of L6 and	
Jun;143(3):524-8 (1990); the contents of each of which are herein incorporated by reference in their entirety.  Exemplary myoblast cells that may be used according to these assays include the rat myoblast L6 cells are an adherent rat myoblast cells are an adherent rat myoblast cell line. Rat myoblast L6 cells are an adherent rat myoblast cell line, isolated from primary cultures of rat thigh muscle, that fuse to form multinucleated myotubes and striated fibers after culture in differentiation media.  HDPGI49 1060 Activation of Kimase assay. INK and p38 Endothelial Cell kinase assay. INK and p38 Endothelial Cell kinase assays for signal apoptosis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including					embryonic porcine myogenic	
contents of each of which are herein incorporated by reference in their entirety.  Exemplary myoblast cells that may be used according to these assays include the rat myoblast L6 cells are an adherent rat myoblast cell line. Rat myoblast L6 cells are an adherent rat myoblast cell line, isolated from primary cultures of rat thigh muscle, that fuse to form multinucleated myotubes and striated fibers after culture in differentiation media.  HDPGI49 1060 Activation of Kinase assay. JNK and p38 Endothelial Cell kinase assays for signal p38 or JNK Signaling Pathway. proliferation, activation, or apoptosis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including					Jun;143(3):524-8 (1990); the	
HDPGI49 1060 Activation of Kinase assays for signal pathway.  End plate the may be used according to these assays include the rat myoblast L6 cells are an adherent rat myoblast cell line. Rat myoblast L6 cells are an adherent rat myoblast cell line, isolated from primary cultures of rat thigh muscle, that firse to form multinucleated myotubes and striated fibers after culture in differentiation media.  Endothelial Cell kinase assay. JNK and p38 Endothelial Cell kinase assays for signal transduction that regulate cell Signaling Pathway. proliferation, activation, or apoptosis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including					contents of each of which are	
reference in their entirety.  Exemplary myoblast cells that may be used according to these assays include the rat myoblast L6 cells are an adherent rat myoblast cell line. Rat myoblast L6 cells are an adherent rat myoblast cell line, isolated from primary cultures of rat thigh muscle, that fuse to form multinucleated myotubes and striated fibers after culture in differentiation media.  HDPG149 1060 Activation of Kinase assay. INK and p38 Endothelial Cell kinase assays for signal transduction that regulate cell Signaling Pathway.  Signaling Pathway. proliferation, activation, or apoptosis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including					herein incorporated by	
Exemplary myoblast cells that may be used according to these assays include the rat myoblast L6 cells are an adherent rat myoblast cell line. Rat myoblast L6 cells are an adherent rat myoblast cell line, isolated from primary cultures of rat thigh muscle, that fuse to form multinucleated myotubes and striated fibers after culture in differentiation media.  HDPG149 1060 Activation of Kinase assay. JNK and p38 Endothelial Cell kinase assays for signal transduction that regulate cell Signaling Pathway. proliferation, activation, or apoptosis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including					reference in their entirety.	
may be used according to these assays include the rat myoblast L6 cell line. Rat myoblast L6 cells are an adherent rat myoblast cell line, isolated from primary cultures of rat thigh muscle, that fuse to form multinucleated myotubes and striated fibers after culture in differentiation media.  HDPGI49 1060 Activation of Kinase assay. INK and p38 Endothelial Cell kinase assays. In K and p38 Endothelial Cell kinase assays for signal p38 or JNK proliferation, activation, or apoptosis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including					Exemplary myoblast cells that	
assays include the rat myoblast L6 cell line. Rat myoblast L6 cells are an adherent rat myoblast cell line, isolated from primary cultures of rat thigh muscle, that fuse to form multinucleated myotubes and striated fibers after culture in differentiation media.  HDPG149 1060 Activation of Kinase assay. JNK and p38 Endothelial Cell kinase assays for signal p38 or JNK signaling Pathway. proliferation, activation, or apoptosis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including					may be used according to these	
HDPG149 1060 Activation of Kinase assay. JNK and p38 Endothelial Cell kinase assays for signal p38 or JNK Signaling Pathway. proliferation, activation, or apoptosis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including					assays include the rat myoblast	
HDPGI49 1060 Activation of Kinase assays. JNK and p38 Endothelial Cell kinase assays for signal p38 or JNK Signaling Pathway. proliferation, activation, or apoptosis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including					L6 cell line. Rat myoblast L6	
HDPGI49 1060 Activation of Kinase assay. JNK and p38 Endothelial Cell kinase assays for signal p38 or JNK Signaling Pathway. Signaling Pathway. Proliferation, activation, or apoptosis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including					cells are an adherent rat	
HDPGI49 1060 Activation of Kinase assay. JNK and p38 Endothelial Cell kinase assays for signal p38 or JNK Signaling Pathway. proliferation, activation, or apoptosis are well known in the art and may be used or routinely modified to assess the invention (including table).					myoblast cell line, isolated	
HDPGI49 1060 Activation of Kinase assay. JNK and p38 Endothelial Cell kinase assays for signal p38 or JNK Signaling Pathway. proliferation, activation, or apoptosis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including					from primary cultures of rat	
HDPGI49 1060 Activation of Kinase assay. JNK and p38 Endothelial Cell kinase assays for signal p38 or JNK Signaling Pathway. proliferation, activation, or apoptosis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including					thigh muscle, that fuse to form	
HDPGI49 1060 Activation of Kinase assay. JNK and p38 Endothelial Cell kinase assays for signal p38 or JNK Signaling Pathway. proliferation, activation, or apoptosis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including					multinucleated myotubes and	
HDPGI49 1060 Activation of Kinase assay. JNK and p38 Endothelial Cell kinase assays for signal p38 or JNK Signaling Pathway. proliferation, activation, or apoptosis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including					striated fibers after culture in	
HDPGI49 1060 Activation of Kinase assay. JNK and p38 Endothelial Cell kinase assays for signal p38 or JNK Signaling Pathway. proliferation, activation, or apoptosis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including					differentiation media.	
Endothelial Cell kinase assays for signal p38 or JNK Signaling Pathway. proliferation, activation, or apoptosis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including		HDPGI49	1060	Activation of	Kinase assay. JNK and p38	A highly preferred
athway. proliferation, activation, or apoptosis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including	7			Endothelial Cell	kinase assays for signal	embodiment of the invention
proliferation, activation, or apoptosis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including				p38 or JNK	transduction that regulate cell	includes a method for
<b></b>				Signaling Pathway.	proliferation, activation, or	stimulating endothelial cell
					apoptosis are well known in	growth. An alternative highly
					the art and may be used or	preferred embodiment of the
					routinely modified to assess	invention includes a method
					the ability of polypeptides of	for inhibiting endothelial cell
_					the invention (including	growth. A highly preferred

	antibodies and agonists or	embodiment of the invention
	antagonists of the invention) to	includes a method for
Id .	promote or inhibit cell	stimulating endothelial cell
ıd	proliferation, activation, and	proliferation. An alternative
	apoptosis. Exemplary assays	highly preferred embodiment
 oj	for JNK and p38 kinase	of the invention includes a
ac	activity that may be used or	method for inhibiting
 	routinely modified to test JNK	endothelial cell proliferation.
 ar	and p38 kinase-induced	A highly preferred
	activity of polypeptides of the	embodiment of the invention
ui	invention (including antibodies	includes a method for
ar	and agonists or antagonists of	stimulating apoptosis of
th	the invention) include the	endothelial cells. An
 	assays disclosed in Forrer et	alternative highly preferred
al	al., Biol Chem 379(8-9):1101-	embodiment of the invention
	1110 (1998); Gupta et al., Exp	includes a method for
<u> </u>	Cell Res 247(2): 495-504	inhibiting (e.g., decreasing)
<u> </u>	(1999); Kyriakis JM, Biochem	apoptosis of endothelial cells.
<u> </u>	Soc Symp 64:29-48 (1999);	A highly preferred
<u> </u>	Chang and Karin, Nature	embodiment of the invention
 4	410(6824):37-40 (2001); and	includes a method for
 <u> </u>	Cobb MH, Prog Biophys Mol	stimulating (e.g., increasing)
 	Biol 71(3-4):479-500 (1999);	endothelial cell activation. An
 th	the contents of each of which	alternative highly preferred
 aı	are herein incorporated by	embodiment of the invention
 re	reference in its entirety.	includes a method for
<u> </u>	Endothelial cells that may be	inhibiting (e.g., decreasing) the
in	used according to these assays	activation of and/or
ar	are publicly available (e.g.,	inactivating endothelial cells.
th	through the ATCC).	A highly preferred
E	Exemplary endothelial cells	embodiment of the invention

that may be used according to these assays include human umbilited vaine and the value and the value and v
that may be used according to these assays include human umbilical vein endothelial cells (HUVEC), which are endothelial cells which line venous blood vessels, and are involved in functions that include, but are not limited to, angiogenesis, vascular permeability, vascular tone, and immune cell extravasation.

hemangioendothelioma,	angiosarcoma,	haemangiopericytoma,	lymphangioma,	lymphangiosarcoma. Highly	preferred indications also	include cancers such as,	prostate, breast, lung, colon,	pancreatic, esophageal,	stomach, brain, liver, and	urinary cancer. Preferred	indications include benign	dysproliferative disorders and	pre-neoplastic conditions, such	as, for example, hyperplasia,	metaplasia, and/or dysplasia.	Highly preferred indications	also include arterial disease,	such as, atherosclerosis,	hypertension, coronary artery	disease, inflammatory	vasculitides, Reynaud's	disease and Reynaud"s	phenomenom, aneurysms,	restenosis; venous and	lymphatic disorders such as	thrombophlebitis,	lymphangitis, and	lymphedema; and other	vascular disorders such as	peripheral vascular disease,
									-											-	_									
	_		•				•••														•									
																							-							

and cancer. Highly	preferred indications also	include trauma such as	wounds, burns, and injured	tissue (e.g., vascular injury	such as, injury resulting from	balloon angioplasty, and	atheroschlerotic lesions),	implant fixation, scarring,	ischemia reperfusion injury,	rheumatoid arthritis,	cerebrovascular disease, renal	diseases such as acute renal	failure, and osteoporosis.	Additional highly preferred	indications include stroke,	graft rejection, diabetic or	other retinopathies, thrombotic	and coagulative disorders,	vascularitis, lymph	angiogenesis, sexual disorders,	age-related macular	degeneration, and treatment	/prevention of endometriosis	and related conditions.	Additional highly preferred	indications include fibromas,	heart disease, cardiac arrest,	heart valve disease, and	vascular disease.	Preferred indications include
	м																													

				blood disorders (e.g., as described below under
<del></del>				"Immune Activity", "Blood-
				Related Disorders", and/or
				Cardiovascular Disorders"). Preferred indications include
				autoimmune diseases (e.g.,
				rheumatoid arthritis, systemic
				lupus erythematosis, multiple
				sclerosis and/or as described
				below) and
				immunodeficiencies (e.g., as
				described below). Additional
=				preferred indications include
				inflammation and
				inflammatory disorders (such
				as acute and chronic
				inflammatory diseases, e.g.,
				inflammatory bowel disease
				and Crohn's disease), and pain
				management.
HDPGP94	1061	Production of	MIP-1alpha FMAT. Assays	A highly preferred
•		MIP1alpha	for immunomodulatory	embodiment of the invention
			proteins produced by activated	includes a method for
			dendritic cells that upregulate	stimulating MIP1a production.
			monocyte/macrophage and T	An alternative highly preferred
			cell chemotaxis are well	embodiment of the invention
1100			known in the art and may be	includes a method for
			used or routinely modified to	uci
			assess the ability of	MIP1a production. A highly
			polypeptides of the invention	preferred indication is

infection (e.g., an infectious			e   Preferred indications include	blood disorders (e.g., as		"Immune Activity", "Blood-	Related Disorders", and/or	"Cardiovascular Disorders").	Highly preferred indications	include autoimmune diseases	(e.g., rheumatoid arthritis,		T   multiple sclerosis and/or as	e   described below) and	immunodeficiencies (e.g., as	described below). Additional	highly preferred indications	include inflammation and		Preferred indications also	include anemia, pancytopenia,	leukopenia, thrombocytopenia,	3- Hodgkin's disease, acute	lymphocytic anemia (ALL),	plasmacytomas, multiple	myeloma, Burkitt's lymphoma,	arthritis, AIDS, granulomatous	disease, inflammatory bowel	disease, sepsis, neutropenia,	neutrophilia, psoriasis,
(including antibodies and	agonists or antagonists of the	invention) to mediate	immunomodulation, modulate	chemotaxis, and modulate T	cell differentiation. Exemplary	assays that test for	immunomodulatory proteins	evaluate the production of	chemokines, such as	macrophage inflammatory	protein 1 alpha (MIP-1a), and	the activation of	monocytes/macrophages and T	cells. Such assays that may be	used or routinely modified to	test immunomodulatory and	chemotaxis activity of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include assays	disclosed in Miraglia et al., J	Biomolecular Screening 4:193-	204(1999); Rowland et al.,	"Lymphocytes: a practical	approach" Chapter 6:138-160	(2000); Satthaporn and	Eremin, J R Coll Surg Ednb	45(1):9-19 (2001); Drakes et	al., Transp Immunol 8(1):17-

				29 (2000); Verhasselt et al., J	suppression of immune reactions to transplanted
				(1997); and Nardelli et al., J	organs and tissues, hemophilia,
				Leukoc Biol 65:822-828	hypercoagulation, diabetes
				(1999), the contents of each of	mellitus, endocarditis,
				which are herein incorporated	meningitis, Lyme Disease,
				by reference in its entirety.	asthma, and allergy.
				Human dendritic cells that may	Preferred indications also
				be used according to these	include neoplastic diseases
				assays may be isolated using	(e.g., leukemia, lymphoma,
				techniques disclosed herein or	and/or as described below
				otherwise known in the art.	under "Hyperproliferative
				Human dendritic cells are	Disorders"). Highly preferred
				antigen presenting cells in	indications include neoplasms
		V		suspension culture, which,	and cancers, such as, leukemia,
				when activated by antigen	lymphoma, prostate, breast,
				and/or cytokines, initiate and	lung, colon, pancreatic,
				upregulate T cell proliferation	esophageal, stomach, brain,
				and functional activities.	liver, and urinary cancer. Other
					preferred indications include
					benign dysproliferative
					disorders and pre-neoplastic
					conditions, such as, for
					example, hyperplasia,
					metaplasia, and/or dysplasia.
	HDPGP94	1061	Production of TNF	TNFa FMAT. Assays for	A highly preferred
113			alpha by dendritic	immunomodulatory proteins	embodiment of the invention
			cells	produced by activated	includes a method for
				macrophages, T cells,	inhibiting (e.g., decreasing)
				fibroblasts, smooth muscle,	TNF alpha production. An
				and other cell types that exert a	alternative highly preferred

	wide variety of inflammatory	embodiment of the invention
	and cytotoxic effects on a	includes a method for
	variety of cells are well known	stimulating (e.g. increasing)
	in the art and may be used or	TNF alpha production
 	routinely modified to assess	Highly preferred indications
	the ability of polypeptides of	include blood disorders (e.g.,
	the invention (including	as described below under
 	antibodies and agonists or	"Immune Activity", "Blood-
	antagonists of the invention) to	Related Disorders", and/or
,	mediate immunomodulation,	"Cardiovascular Disorders"),
	modulate inflammation and	Highly preferred indications
	cytotoxicity. Exemplary	include autoimmune diseases
 	assays that test for	(e.g., rheumatoid arthritis,
	immunomodulatory proteins	systemic lupus erythematosis,
	evaluate the production of	Crohn"s disease, multiple
-	cytokines such as tumor	sclerosis and/or as described
	necrosis factor alpha (TNFa),	below), immunodeficiencies
	and the induction or inhibition	(e.g., as described below),
	of an inflammatory or	boosting a T cell-mediated
	cytotoxic response. Such	immune response, and
	assays that may be used or	suppressing a T cell-mediated
	routinely modified to test	immune response. Additional
	immunomodulatory activity of	highly preferred indications
	polypeptides of the invention	include inflammation and
	(including antibodies and	inflammatory disorders, and
	agonists or antagonists of the	treating joint damage in
	invention) include assays	patients with rheumatoid
	disclosed in Miraglia et al., J	arthritis. An additional highly
	Biomolecular Screening 4:193-	preferred indication is sepsis.
	204(1999); Rowland et al.,	Highly preferred indications
	"Lymphocytes: a practical	include neoplastic diseases

					reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, cardiac reperfusion injury, and asthma and allergy. An additional preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease").
114	HDPHI51	1062	Regulation of transcription through the FAS promoter element in hepatocytes	Assays for the regulation of transcription through the FAS promoter element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to activate the FAS promoter element in a reporter construct and to regulate transcription of FAS, a key enzyme for lipogenesis. FAS promoter is regulated by many transcription factors including SREBP. Insulin increases FAS gene transcription in livers of diabetic mice. This	A highly preferred indication is diabetes mellitus. An additional highly preferred indication is a complication associated with diabetes (e.g., diabetic retinopathy, diabetic nephropathy, kidney disease (e.g., renal failure, nephropathy and/or other diseases and disorders as described in the "Renal Disorders" section below), diabetic neuropathy, nerve disease and nerve damage (e.g., due to diabetic neuropathy), blood vessel blockage, heart disease, stroke, impotence (e.g., due to diabetic neuropathy or blood vessel blockage), seizures, mental

	also somewhat glucose	confusion, drowsiness,
	dependent. Exemplary assays	nonketotic hyperglycemic-
	that may be used or routinely	hyperosmolar coma,
	modified to test for FAS	cardiovascular disease (e.g.,
	promoter element activity (in	heart disease, atherosclerosis,
	hepatocytes) by polypeptides	microvascular disease,
	of the invention (including	hypertension, stroke, and other
	antibodies and agonists or	diseases and disorders as
	antagonists of the invention)	described in the
	include assays disclosed in	"Cardiovascular Disorders"
 	Xiong, S., et al., Proc Natl	section below), dyslipidemia,
	Acad Sci U.S.A., 97(8):3948-	endocrine disorders (as
	53 (2000); Roder, K., et al.,	described in the "Endocrine
	Eur J Biochem, 260(3):743-51	Disorders" section below),
	(1999); Oskouian B, et al.,	neuropathy, vision impairment
	Biochem J, 317 (Pt 1):257-65	(e.g., diabetic retinopathy and
 	(1996); Berger, et al., Gene	blindness), ulcers and impaired
	66:1-10 (1988); and, Cullen,	wound healing, and infection
 	B., et al., Methods in Enzymol.	(e.g., infectious diseases and
	216:362–368 (1992), the	disorders as described in the
	contents of each of which is	"Infectious Diseases" section
	herein incorporated by	below, especially of the
	reference in its entirety.	urinary tract and skin), carpal
	Hepatocytes that may be used	tunnel syndrome and
	according to these assays, such	Dupuytren's contracture).
	as H4IIE cells, are publicly	An additional highly preferred
	available (e.g., through the	indication is obesity and/or
	ATCC) and/or may be	complications associated with
	routinely generated.	obesity. Additional highly
	Exemplary hepatocytes that	preferred indications include
	may be used according to these   weight loss or alternatively,	weight loss or alternatively,

				assays include rat liver	weight gain. Aditional
				hepatoma cell line(s) inducible	highly preferred indications are
				with glucocorticoids, insulin,	complications associated with
				or cAMP derivatives.	insulin resistance.
	HDPHI51	1062	Activation of	Assays for the activation of	A highly preferred
114			transcription	transcription through the	indication is allergy.
			through STAT6	Signal Transducers and	Another highly preferred
			response element in	Activators of Transcription	indication is asthma.
			immune cells (such	(STAT6) response element are	Additional highly preferred
	-		as T-cells).	well-known in the art and may	indications include
				be used or routinely modified	inflammation and
				to assess the ability of	inflammatory disorders.
				polypeptides of the invention	Preferred indications include
				(including antibodies and	blood disorders (e.g., as
				agonists or antagonists of the	described below under
				invention) to regulate STAT6	"Immune Activity", "Blood-
				transcription factors and	Related Disorders", and/or
	-			modulate the expression of	"Cardiovascular Disorders").
				multiple genes. Exemplary	Preferred indications include
				assays for transcription	autoimmune diseases (e.g.,
				through the STAT6 response	rheumatoid arthritis, systemic
				element that may be used or	lupus erythematosis, multiple
				routinely modified to test	sclerosis and/or as described
				STAT6 response element	below) and
				activity of the polypeptides of	immunodeficiencies (e.g., as
				the invention (including	described below).
				antibodies and agonists or	Preferred indications include
				antagonists of the invention)	neoplastic diseases (e.g.,
				include assays disclosed in	leukemia, lymphoma,
				Berger et al., Gene 66:1-10	melanoma, and/or as described
				(1998); Cullen and Malm,	below under

"Hyperproliferative Disorders"). Preferred	indications include neoplasms	and cancers, such as, leukemia,	lymphoma, melanoma, and	prostate, breast, lung, colon,	pancreatic, esophageal,	stomach, brain, liver and	urinary cancer. Other preferred	indications include benign	dysproliferative disorders and	pre-neoplastic conditions, such	as, for example, hyperplasia,	metaplasia, and/or dysplasia.	Preferred indications include	anemia, pancytopenia,	leukopenia, thrombocytopenia,	Hodgkin's disease, acute	lymphocytic anemia (ALL),	plasmacytomas, multiple	myeloma, Burkitt's lymphoma,	arthritis, AIDS, granulomatous	disease, inflammatory bowel	disease, sepsis, neutropenia,	neutrophilia, psoriasis,	suppression of immune	reactions to transplanted	organs and tissues,	hemophilia, hypercoagulation,	diabetes mellitus, endocarditis,	meningitis, and Lyme Disease.
Methods in Enzymol 216:362-368 (1992): Henthorn et al	Proc Natl Acad Sci USA	85:6342-6346 (1988); Georas	et al., Blood 92(12):4529-4538	(1998); Moffatt et al.,	Transplantation 69(7):1521-	1523 (2000); Curiel et al., Eur	J Immunol 27(8):1982-1987	(1997); and Masuda et al., J	Biol Chem 275(38):29331-	29337 (2000), the contents of	each of which are herein	incorporated by reference in its	entirety. T cells that may be	used according to these assays	are publicly available (e.g.,	through the ATCC).	Exemplary T cells that may be	used according to these assays	include the SUPT cell line,	which is a suspension culture	of IL-2 and IL-4 responsive T	cells.							
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					An additional preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease").
	HDPJF37	1063	Activation of	Assays for the activation of	Highly preferred indications
1115	•		transcription	transcription through the	include blood disorders (e.g.,
		,	response in immune	cells (NFAT) response element	"Immune Activity", "Blood-
			cells (such as T-	are well-known in the art and	Related Disorders", and/or
			cells).	may be used or routinely	"Cardiovascular Disorders").
				modified to assess the ability	Highly preferred indications
			-	of polypeptides of the	include autoimmune diseases
				invention (including antibodies	(e.g., rheumatoid arthritis,
				and agonists or antagonists of	systemic lupus erythematosis,
				the invention) to regulate	multiple sclerosis and/or as
				NFAT transcription factors and	described below),
				modulate expression of genes	immunodeficiencies (e.g., as
				involved in	described below), boosting a T
				immunomodulatory functions.	cell-mediated immune
				Exemplary assays for	response, and suppressing a T
				transcription through the	cell-mediated immune
				NFAT response element that	response. Additional highly
				may be used or routinely	preferred indications include
				modified to test NFAT-	inflammation and
		,		response element activity of	inflammatory disorders. An
				polypeptides of the invention	additional highly preferred
				(including antibodies and	indication is infection (e.g., an
				agonists or antagonists of the	infectious disease as described
				invention) include assays	below under "Infectious
				disclosed in Berger et al., Gene	Disease"). Preferred

indications include neoplastic	diseases (e.g., leukemia,	lymphoma, and/or as described	below under	Hyperproliferative	Disorders"). Preferred	indications include neoplasms	and cancers, such as, for	example, leukemia, lymphoma,	and prostate, breast, lung,	colon, pancreatic, esophageal,	stomach, brain, liver and	urinary cancer. Other preferred	indications include benign	dysproliferative disorders and	pre-neoplastic conditions, such	as, for example, hyperplasia,	metaplasia, and/or dysplasia.	Preferred indications also	include anemia, pancytopenia,	leukopenia, thrombocytopenia,		lymphocytic anemia (ALL),	plasmacytomas, multiple	myeloma, Burkitt's lymphoma,	arthritis, AIDS, granulomatous	disease, inflammatory bowel	disease, sepsis, neutropenia,	neutrophilia, psoriasis,	suppression of immune	reactions to transplanted
66:1-10 (1998); Cullen and	Malm, Methods in Enzymol	216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA	85:6342-6346 (1988); Serfling	et al., Biochim Biophys Acta	1498(1):1-18 (2000); De Boer	et al., Int J Biochem Cell Biol	31(10):1221-1236 (1999);	Fraser et al., Eur J Immunol	29(3):838-844 (1999); and	Yeseen et al., J Biol Chem	268(19):14285-14293 (1993),	the contents of each of which	are herein incorporated by	reference in its entirety. T	cells that may be used	according to these assays are	publicly available (e.g.,	through the ATCC).	Exemplary human T cells that	may be used according to these	assays include the JURKAT	cell line, which is a suspension	culture of leukemia cells that	produce IL-2 when stimulated.					
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					organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, asthma and allergy.
116	HDPMM88	1064	Myoblast cell proliferation	Assays for muscle cell proliferation are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to stimulate or inhibit myoblast cell proliferation. Exemplary assays for myoblast cell proliferation that may be used or routinely modified to test activity of polypeptides and antibodies of the invention (including agonists or antagonists of the invention) include, for example, assays disclosed in: Soeta, C., et al. "Possible role for the c-ski gene in the proliferation of myogenic cells in regenerating skeletal muscles of rats" Dev Growth Differ Apr;43(2):155-64 (2001); Ewton DZ, et al., "IGF binding proteins.4 -5	Highly preferred indications include diabetes, myopathy, muscle cell atrophy, cancers of muscle (such as, rhabdomyoma, and rhabdosarcoma), cardiovascular disorders (such as congestive heart failure, cachexia, myxomas, fibromas, congenital cardiovascular abnormalities, heart disease, cardiac arrest, heart valve disease, vascular disease, and also as described below under "Cardiovascular Disorders"), stimulating myoblast proliferation.

and -6 may play specialized roles during L6 myoblast proliferation and differentiation." J Endocrinol Mar,144(3):539-53 (1995); and, Pampusch MS, et al.,"Effect of transforming growth factor beta on proliferation of L6 and embryonic porcine myogenic cells." J Cell Physiol Jun;143(3):524-8 (1990); the contents of each of which are herein incorporated by reference in their entirety. Exemplary myoblast cells that may be used according to these assays include the rat myoblast L6 cells are an adherent rat myoblast cell line. Rat myoblast L6 cells are an adherent rat myoblast cell line, isolated from primary cultures of rat thigh muscle, that fuse to form multinucleated myotubes and striated fibers after culture in differentiation media.	This reporter assay measures activation or inhibition of the NFkB signaling pathway in Ku812 human basophil cell line. Assays for the activation
	Activation or inhibition of transcription through NFKB response element in
	1064
	HDPMM88
	116

or inhibition of transcription	through the NFKB response	element are well-known in the	art and may be used or	routinely modified to assess	the ability of polypeptides of	the invention (including	antibodies and agonists or	antagonists of the invention) to	regulate NFKB transcription	factors and modulate	expression of	immunomodulatory genes.	NFkB is important in the	pathogenesis of asthma.	Exemplary assays for	transcription through the	NFKB response element that	may be used or rountinely	modified to test NFKB-	response element activity of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include assays	disclosed in Berger et al., Gene	66:1-10 (1998); Cullen and	Malm, Methods in Enzymol	216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA	85:6342-6346 (1988); Marone
immune cells (such	as basophils).																<del></del>													

et al, Int Arch Allergy Immunol 114(3):207-17 (1997), the contents of each of which are herein incorporated by reference in its entirety.	Cells were pretreated with SID supernatants or controls for 15-18 hours, and then 10 ng/mL of TNF was added to stimulate the NFkB reporter. SEAP	activity was measured after 48 hours. Basophils that may be used according to these assays are publicly available (e.g., through the ATCC).	Exemplary human basophil cell lines that may be used according to these assays include Ku812, originally established from a patient with chronic myelogenous	leukemia. It is an immature prebasophilic cell line that can be induced to differentiate into mature basophils. See, Kishi et al., Leuk Res. 9:381-390 (1985); Blom et al., Eur J Immunol. 22:2025-32 (1992), where the contents of each are	herein incorporated by reference in its entirety.

	HDPNC61	1065	Activation of	Assays for the activation of	A highly preferred indication
1117			transcription	transcription through the	is obesity and/or complications
			through cAMP	cAMP response element are	associated with obesity.
٠, -			response element	well-known in the art and may	Additional highly preferred
·			(CRE) in pre-	be used or routinely modified	indications include weight loss
,			adipocytes.	to assess the ability of	or alternatively, weight gain.
				polypeptides of the invention	An additional highly preferred
		-		(including antibodies and	indication is diabetes mellitus.
				agonists or antagonists of the	An additional highly preferred
		-		invention) to increase cAMP,	indication is a complication
				regulate CREB transcription	associated with diabetes (e.g.,
				factors, and modulate	diabetic retinopathy, diabetic
				expression of genes involved	nephropathy, kidney disease
				in a wide variety of cell	(e.g., renal failure,
				functions. For example, a	nephropathy and/or other
				3T3-L1/CRE reporter assay	diseases and disorders as
				may be used to identify factors	described in the "Renal
	,			that activate the cAMP	Disorders" section below),
				signaling pathway. CREB	diabetic neuropathy, nerve
		·		plays a major role in	disease and nerve damage
	-			adipogenesis, and is involved	(e.g., due to diabetic
	·			in differentiation into	neuropathy), blood vessel
				adipocytes. CRE contains the	blockage, heart disease, stroke,
				binding sequence for the	impotence (e.g., due to diabetic
				transcription factor CREB	neuropathy or blood vessel
				(CRE binding protein).	blockage), seizures, mental
				Exemplary assays for	confusion, drowsiness,
				transcription through the	nonketotic hyperglycemic-
				cAMP response element that	hyperosmolar coma,
				may be used or routinely	cardiovascular disease (e.g.,
				modified to test cAMP-	heart disease, atherosclerosis,

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microvascular disease,	hypertension, stroke, and other	diseases and disorders as	described in the	"Cardiovascular Disorders"	section below), dyslipidemia,	endocrine disorders (as	described in the "Endocrine	Disorders" section below),	neuropathy, vision impairment	(e.g., diabetic retinopathy and	blindness), ulcers and impaired	wound healing, and infection	(e.g., infectious diseases and	disorders as described in the	"Infectious Diseases" section	below, especially of the	urinary tract and skin), carpal	tunnel syndrome and	Dupuytren's contracture).	Additional highly preferred	indications are complications	associated with insulin	resistance.				-			
response element activity of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include assays	disclosed in Berger et al., Gene	66:1-10 (1998); Cullen and	Malm, Methods in Enzymol	216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA	85:6342-6346 (1988); Reusch	et al., Mol Cell Biol	20(3):1008-1020 (2000); and	Klemm et al., J Biol Chem	273:917-923 (1998), the	contents of each of which are	herein incorporated by	reference in its entirety. Pre-	adipocytes that may be used	according to these assays are	publicly available (e.g.,	through the ATCC) and/or	may be routinely generated.	Exemplary mouse adipocyte	cells that may be used	according to these assays	include 3T3-L1 cells. 3T3-L1	is an adherent mouse	preadipocyte cell line that is a	continuous substrain of 3T3	fibroblast cells developed
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				through clonal isolation and	
				undergo a pre-adipocyte to	
3				adipose-like conversion under	
				appropriate differentiation	
				conditions known in the art.	
	HDPNC61	1065	Activation of	Assays for the activation of	Highly preferred indications
1117			transcription	transcription through the	include asthma, allergy,
			through GAS	Gamma Interferon Activation	hypersensitivity reactions,
			response element in	Site (GAS) response element	inflammation, and
			immune cells (such	are well-known in the art and	inflammatory disorders.
			as eosinophils).	may be used or routinely	Additional highly preferred
				modified to assess the ability	indications include immune
				of polypeptides of the	and hematopoietic disorders
				invention (including antibodies	(e.g., as described below under
				and agonists or antagonists of	"Immune Activity", and
				the invention) to modulate	"Blood-Related Disorders"),
	-			gene expression (commonly	autoimmune diseases (e.g.,
				via STAT transcription factors)	rheumatoid arthritis, systemic
_				involved in a wide variety of	lupus erythematosis, Crohn"s
				cell functions. Exemplary	disease, multiple sclerosis
				assays for transcription	and/or as described below),
				through the GAS response	immunodeficiencies (e.g., as
				element that may be used or	described below), boosting an
				routinely modified to test	eosinophil-mediated immune
				GAS-response element activity	response and, alternatively,
				of polypeptides of the	suppressing an eosinophil-
				invention (including antibodies	mediated immune response.
				and agonists or antagonists of	
				the invention) include assays	
				disclosed in Berger et al., Gene	
				66:1-10 (1998); Cullen and	

Malm, Methods in Enzymol 216:362-368 (1992); Henthorn	85:6342-6346 (1988);	Matikainen et al., Blood 93(6):1980-1991 (1999); and	Henttinen et al., J Immunol	155(10):4582-4587 (1995); the	contents of each of which are	herein incorporated by	reference in its entirety.	Moreover, exemplary assays	that may be used or routinely	modified to assess the ability	of polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) to activate or	inhibit activation of immune	cells include assays disclosed	and/or cited in: Mayumi M.,	"EoL-1, a human eosinophilic	cell line" Leuk Lymphoma;	Jun;7(3):243-50 (1992);	Bhattacharya S, "Granulocyte	macrophage colony-	stimulating factor and	interleukin-5 activate STAT5	and induce CIS1 mRNA in	human peripheral blood	eosinophils" Am J Respir Cell
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	A highly preferred embodiment of the invention includes a method for stimulating endothelial cell growth. An alternative highly
Mol Biol; Mar;24(3):312-6 (2001); and, Du J, et al., "Engagement of the CrkL adapter in interleukin-5 signaling in eosinophils" J Biol Chem; Oct 20;275(42):33167-75 (2000); the contents of each of which are herein incorporated by reference in its entirety. Exemplary cells that may be used according to these assays include eosinophils. Eosinophils are a type of immune cell important in the late stage of allergic reactions; they are recruited to tissues and mediate the inflammtory response of late stage allergic reaction. Increases in GAS mediated transcription in eosinophils is typically a result of STAT activation, normally a direct consequence of interleukin or other cytokine receptor stimulation (e.g. IL3, IL5 or GMCSF).	Kinase assay. Kinase assays, for example an Elk-1 kinase assay, for ERK signal transduction that regulate cell proliferation or differentiation
	Activation of Endothelial Cell ERK Signaling Pathway.
	1065
	HDPNC61
	117

	invention includes a method	ity   for inhibiting endothelial cell	growth. A highly preferred	odies embodiment of the invention	s of includes a method for	or stimulating endothelial cell	proliferation. An alternative	ion.   highly preferred embodiment		e method for inhibiting	to endothelial cell proliferation.	A highly preferred		odies   includes a method for	s of stimulating apoptosis of		et alternative highly preferred	101- embodiment of the invention	includes a method for	inhibiting (e.g., decreasing)	apoptosis of endothelial cells.	A highly preferred	hang embodiment of the invention	includes a method for	and stimulating (e.g., increasing)	Mol endothelial cell activation. An	99); alternative highly preferred			inhibiting the activation of
are well known in the art and	may be used or routinely	modified to assess the ability	of polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) to promote or	inhibit cell proliferation,	activation, and differentiation.	Exemplary assays for ERK	kinase activity that may be	used or routinely modified to	test ERK kinase-induced	activity of polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) include the	assays disclosed in Forrer et	al., Biol Chem 379(8-9):1101-	1110 (1998); Berra et al.,	Biochem Pharmacol	$\{60(8):1171-1178\ (2000);$	Gupta et al., Exp Cell Res	247(2):495-504 (1999); Chang	and Karin, Nature	410(6824):37-40 (2001); and	Cobb MH, Prog Biophys Mol	Biol 71(3-4):479-500 (1999);	the contents of each of which	are herein incorporated by	reference in its entirety.
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(e.g., decreasing) and/or	inactivating endothelial cells.	A highly preferred	embodiment of the invention	includes a method for	stimulating endothelial cell	differentiation. An alternative	highly preferred embodiment	of the invention includes a	method for inhibiting	endothelial cell differentiation.	A highly preferred	embodiment of the invention	includes a method for	stimulating angiogenisis. An	alternative highly preferred	embodiment of the invention	includes a method for	inhibiting angiogenesis.	A highly preferred	embodiment of the invention	includes a method for reducing	cardiac hypertrophy. An	alternative highly preferred	embodiment of the invention	includes a method for inducing	cardiac hypertrophy. Highly	preferred indications include	neoplastic diseases (e.g., as	described below under	"Hyperproliferative
Endothelial cells that may be	used according to these assays	are publicly available (e.g.,	through the ATCC).	Exemplary endothelial cells	that may be used according to	these assays include human	umbilical vein endothelial cells	(HUVEC), which are	endothelial cells which line	venous blood vessels, and are	involved in functions that	include, but are not limited to,	angiogenesis, vascular	permeability, vascular tone,	and immune cell extravasation.			-												
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Disorders"), and disorders of	the cardiovascular system	(e.g., heart disease, congestive	heart failure, hypertension,	aortic stenosis,	cardiomyopathy, valvular	regurgitation, left ventricular	dysfunction, atherosclerosis	and atherosclerotic vascular	disease, diabetic nephropathy,	intracardiac shunt, cardiac	hypertrophy, myocardial	infarction, chronic	hemodynamic overload, and/or	as described below under	"Cardiovascular Disorders").	Highly preferred indications	include cardiovascular,	endothelial and/or angiogenic	disorders (e.g., systemic	disorders that affect vessels	such as diabetes mellitus, as	well as diseases of the vessels	themselves, such as of the	arteries, capillaries, veins	and/or lymphatics). Highly	preferred are indications that	stimulate angiogenesis and/or	cardiovascularization. Highly	preferred are indications that	inhibit angiogenesis and/or
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cardiovascularization.	Highly preferred indications	include antiangiogenic activity	to treat solid tumors,	leukemias, and Kaposi"s	sarcoma, and retinal disorders.	Highly preferred indications	include neoplasms and cancer,	such as, Kaposi"s sarcoma,	hemangioma (capillary and	cavernous), glomus tumors,	telangiectasia, bacillary	angiomatosis,	hemangioendothelioma,	angiosarcoma,	haemangiopericytoma,	lymphangioma,	lymphangiosarcoma. Highly	preferred indications also	include cancers such as,	prostate, breast, lung, colon,	pancreatic, esophageal,	stomach, brain, liver, and	urinary cancer. Preferred	indications include benign	dysproliferative disorders and	pre-neoplastic conditions, such	as, for example, hyperplasia,	metaplasia, and/or dysplasia.	Highly preferred indications	also include arterial disease,
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such as, atherosclerosis, hypertension, coronary artery disease, inflammatory vasculitides, Reynaud's	disease and Reynaud"s phenomenom, aneurysms, restenosis; venous and lymphatic disorders such as thrombophlebitis, lymphangitis, and	vascular disorders such as peripheral vascular disease, and cancer. Highly preferred indications also include trauma such as wounds, burns, and injured tissue (e.g., vascular injury	such as, injury resulting from balloon angioplasty, and atheroschlerotic lesions), implant fixation, scarring, ischemia reperfusion injury, rheumatoid arthritis, cerebrovascular disease, renal diseases such as acute renal failure, and osteoporosis.  Additional highly preferred indications include stroke,	graft rejection, diabetic or other retinopathies, thrombotic

and coagulative disorders, vascularitis, lymph angiogenesis, sexual disorders, age-related macular degeneration, and treatment /prevention of endometriosis and related conditions.  Additional highly preferred indications include fibromas, heart disease, cardiac arrest, heart valve disease, and vascular disease.  Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders").  Preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic.	lupus erythematosis, multiple sclerosis and/or as described below) and immunodeficiencies (e.g., as described below). Additional preferred indications include inflammation and inflammatory disorders (such as acute and chronic inflammatory diseases, e.g.,

S .	inflammatory bowel disease and Crohn's disease), and pain	management.	Assays for the activation of Highly preferred indications	transcription through the include neoplastic diseases	Gamma Interferon Activation (e.g., leukemia, lymphoma,	Site (GAS) response element	are well-known in the art and		modified to assess the ability indications include neoplasms		ntibodies	 the invention) to regulate Burkitt's lymphoma, non-	STAT transcription factors and Hodgkins lymphoma,	modulate gene expression Hodgkin's disease),	involved in a wide variety of melanoma, and prostate,	cell functions. Exemplary   breast, lung, colon, pancreatic,	assays for transcription esophageal, stomach, brain,	through the GAS response   liver and urinary cancer. Other	ı	routinely modified to test benign dysproliferative	GAS-response element activity   disorders and pre-neoplastic	of polypeptides of the conditions, such as, for	invention (including antibodies   example, hyperplasia,	 the invention) include assays   Preferred indications include	disclosed in Berger et al., Gene   autoimmune diseases (e.g.,	66:1-10 (1998); Cullen and rheumatoid arthritis, systemic	Malm. Methods in Enzymol   lupus erythematosis, multiple
			1065 Activation of		through GAS	response element in	immune cells (such	as T-cells).																			
			HDPNC61							~												-				·	
				1117																							

et al Proc Natl Acad Sci HSA   helow) immunodeficiencies	 þc	93(6):1980-1991 (1999); and immune response, and	Henttinen et al., J Immunol   suppressing a T cell-mediated	the	contents of each of which are preferred indications include	herein incorporated by inflammation and	reference in its entirety. inflammatory disorders.	Exemplary human T cells, Highly preferred indications	such as the MOLT4 cell line, include blood disorders (e.g.,	that may be used according to as described below under	these assays are publicly "Immune Activity", "Blood-	Je	ATCC). ("Cardiovascular Disorders"),	and infection (e.g., viral	infections, tuberculosis,	infections associated with	chronic granulomatosus	disease and malignant	osteoporosis, and/or an	infectious disease as described	below under "Infectious	Disease"). An additional	preferred indication is	idiopathic pulmonary fibrosis.	Preferred indications include	anemia, pancytopenia,	leukopenia, thrombocytopenia,	acute lymphocytic anemia

multiple myeloma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, and asthma and allergy.	eins of T wn in or sess ses of ion) to tion, or set for eins of TES.
	RANTES FMAT. Assays for immunomodulatory proteins that induce chemotaxis of T cells, monocytes, and eosinophils are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mediate immunomodulation, induce chemotaxis, and/or mediate humoral or cellmediate humoral or cellmediated immunity.  Exemplary assays that test for immunomodulatory proteins evaluate the production of cytokines, such as RANTES,
	Production of RANTES in bronchial epithelium cells
	1065
	HDPNC61
	117

and the induction of	chemotactic responses in	immune cells. Such assays	that may be used or routinely	modified to test	immunomodulatory activity of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include the assays	disclosed in Miraglia et al., J	Biomolecular Screening 4:193-	204 (1999); Rowland et al.,	"Lymphocytes: a practical	approach" Chapter 6:138-160	(2000): Cocchi et al., Science	270(5243):1811-1815 (1995);	and Robinson et al., Clin Exp	Immunol 101(3):398-407	(1995), the contents of each of	which are herein incorporated	by reference in its entirety.	Epithelial cells were isolated	from bronchia/trachea	immediately postmortem from	humans who were free of	known respiratory diseases.	See Wu et al., Am Rev Respir	Dis. 132(2):311-20 (1985), the	contents of which are herein	incorporated by reference in its
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				entirety.	
	HDPND46	1066	Activation of	Kinase assay. Kinase assays,	A highly preferred
118			Adipocyte PI3	for example an GSK-3 assays,	embodiment of the invention
	<u> </u>		Kinase Signalling	for PI3 kinase signal	includes a method for
	· · · · · · · · · · · · · · · · · · ·		Pathway	transduction that regulate	increasing adipocyte survival
				glucose metabolism and cell	An alternative highly preferred
	·			survival are well-known in the	embodiment of the invention
	s			art and may be used or	includes a method for
				routinely modified to assess	decreasing adipocyte survival.
		,		the ability of polypeptides of	A preferred embodiment of the
				the invention (including	invention includes a method
				antibodies and agonists or	for stimulating adipocyte
				antagonists of the invention) to	proliferation. An alternative
	· · ·			promote or inhibit glucose	highly preferred embodiment
				metabolism and cell survival.	of the invention includes a
				Exemplary assays for PI3	method for inhibiting
				kinase activity that may be	adipocyte proliferation. A
				used or routinely modified to	preferred embodiment of the
·				test PI3 kinase-induced activity	invention includes a method
				of polypeptides of the	for stimulating adipocyte
				invention (including antibodies	differentiation. An alternative
				and agonists or antagonists of	highly preferred embodiment
				the invention) include assays	of the invention includes a
				disclosed in Forrer et al., Biol	method for inhibiting
				Chem 379(8-9):1101-1110	adipocyte differentiation.
				(1998); Nikoulina et al.,	Highly preferred indications
				Diabetes 49(2):263-271	include endocrine disorders
				(2000); and Schreyer et al.,	(e.g., as described below under
				Diabetes 48(8):1662-1666	"Endocrine Disorders").
				(1999), the contents of each of	Preferred indications include
				which are herein incorporated	neoplastic diseases (e.g.,

	by reference in its entirety.	lipomas, liposarcomas, and/or
	Mouse adinocyte cells that	as described below under
-	may be used according to these	"Hymermoliferative
	occours one with light original	Discordens? Hood discordens
	assays are publicly available	Disorders ), blood disorders
	(e.g., through the ATCC).	(e.g., hypertension, congestive
	Exemplary mouse adipocyte	heart failure, blood vessel
	cells that may be used	blockage, heart disease, stroke,
	according to these assays	impotence and/or as described
	include 3T3-L1 cells. 3T3-L1	below under "Immune
	is an adherent mouse	Activity", "Cardiovascular
	preadipocyte cell line that is a	Disorders", and/or "Blood-
	continous substrain of 3T3	Related Disorders"), immune
	fibroblast cells developed	disorders (e.g., as described
	through clonal isolation and	below under "Immune
	undergo a pre-adipocyte to	Activity"), neural disorders
	adipose-like conversion under	(e.g., as described below under
	appropriate differentiation	"Neural Activity and
	conditions known in the art.	Neurological Diseases"), and
		infection (e.g., as described
		below under "Infectious
		Disease"). A highly
		preferred indication is diabetes
		mellitus. An additional
		highly preferred indication is a
		complication associated with
		diabetes (e.g., diabetic
		retinopathy, diabetic
		nephropathy, kidney disease
		(e.g., renal failure,
		nephropathy and/or other
		diseases and disorders as

	described in the "Renal	Disorders" section below),	diabetic neuropathy, nerve	disease and nerve damage (e.g.	due to diabetic neuropathy),	blood vessel blockage, heart	disease, stroke, impotence	(e.g., due to diabetic	neuropathy or blood vessel	blockage), seizures, mental	confusion, drowsiness,	nonketotic hyperglycemic-	hyperosmolar coma,	cardiovascular disease (e.g.,	heart disease, atherosclerosis,	microvascular disease,	hypertension, stroke, and other	diseases and disorders as	described in the	"Cardiovascular Disorders"	section below), dyslipidemia,	endocrine disorders (as	described in the "Endocrine	Disorders" section below),	neuropathy, vision impairment	(e.g., diabetic retinopathy and	blindness), ulcers and impaired	wound healing, infection (e.g.,	infectious diseases and	disorders as described in the	
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helow esnecially of the	urinary tract and skin), carpal	tunnel syndrome and	Dupuytren's contracture).	An additional highly preferred	indication is obesity and/or	complications associated with	obesity. Additional highly	preferred indications include	weight loss or alternatively,	weight gain. Additional	highly preferred indications are	complications associated with	insulin resistance.	Additional highly preferred	indications are disorders of the	musculoskeletal systems	including myopathies,	muscular dystrophy, and/or as	described herein.	Additional highly preferred	indications include,	hypertension, coronary artery	disease, dyslipidemia,	gallstones, osteoarthritis,	degenerative arthritis, eating	disorders, fibrosis, cachexia,	and kidney diseases or	disorders. Highly preferred	indications include neonlocms
	•																												
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					liposarcoma, lymphoma, leukemia and breast, colon, and kidney cancer. Additional highly preferred indications include melanoma, prostate, lung, pancreatic, esophageal, stomach, brain, liver, and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia.
118	HDPND46	1066	Production of IL-4	IL-4 FMAT. Assays for immunomodulatory proteins secreted by TH2 cells that stimulate B cells, T cells, macrophages and mast cells and promote polarization of CD4+ cells into TH2 cells are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mediate immunomodulation, stimulate immune cells, modulate immune cells, modulate	A highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing) IL-4 production. An alternative highly preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) IL-4 production. A highly preferred indication includes asthma. A highly preferred indication includes allergy. A highly preferred indication includes rhinitis. Additional highly preferred indications include
		·		and/or mediate humoral or	inflammatory disorders.

cell-mediated immunity.	Highly preferred indications
 Exemplary assays that test for	include neoplastic diseases
immunomodulatory proteins	(e.g., leukemia, lymphoma,
evaluate the production of	melanoma, and/or as described
cytokines, such as IL-4, and	below under
the stimulation of immune	"Hyperproliferative
cells, such as B cells, T cells,	Disorders"). Preferred
macrophages and mast cells.	indications include neoplasms
Such assays that may be used	and cancers, such as, for
 or routinely modified to test	example, leukemia, lymphoma,
immunomodulatory activity of	melanoma, and prostate,
polypeptides of the invention	breast, lung, colon, pancreatic,
(including antibodies and	esophageal, stomach, brain,
agonists or antagonists of the	liver and urinary cancer. Other
 invention) include the assays	preferred indications include
 disclosed in Miraglia et al., J	benign dysproliferative
 Biomolecular Screening 4:193-	disorders and pre-neoplastic
204 (1999); Rowland et al.,	conditions, such as, for
"Lymphocytes: a practical	example, hyperplasia,
approach" Chapter 6:138-160	metaplasia, and/or dysplasia.
(2000); Gonzalez et al., J Clin	Preferred indications include
Lab Anal 8(5):277-283 (1194);	blood disorders (e.g., as
Yssel et al., Res Immunol	described below under
144(8):610-616 (1993); Bagley	"Immune Activity", "Blood-
et al., Nat Immunol 1(3):257-	Related Disorders", and/or
261 (2000); and van der Graaff	"Cardiovascular Disorders").
et al., Rheumatology (Oxford)	Preferred indications include
38(3):214-220 (1999), the	autoimmune diseases (e.g.,
contents of each of which are	rheumatoid arthritis, systemic
herein incorporated by	lupus erythematosis, multiple
reference in its entirety.	sclerosis and/or as described

				Human T cells that may be used according to these assays may be isolated using techniques disclosed herein or otherwise known in the art. Human T cells are primary human lymphocytes that mature in the thymus and express a T cell receptor and CD3, CD4, or CD8. These cells mediate humoral or cellmediated immunity and may be preactivated to enhance responsiveness to immunomodulatory factors.	below) and immunodeficiencies (e.g., as described below). Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, and Lyme Disease. An additonal preferred indication is infectious disease as described below under "Infectious
118	HDPND46	1066	Production of IL-8 by by endothelial cells (such as Human Umbilical Cord Endothelial Cells).	Assays measuring production of IL-8 are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including	Highly preferred indications include immunological and inflammatory disorders (e.g., such as allergy, asthma, leukemia, etc. and as described below under "Immune

		1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1
	annoonies and agomists or	Activity, and blood-Kelated
	antagonists of the invention) to	Disorders"). Highly preferred
	regulate production and/or	indications also includie
	secretion of IL-8. For	autoimmune disorders (e.g.,
	example, FMAT may be used	rheumatoid arthritis, systemic
	or routinely modified to assess	lupus erythematosis, Crohn"s
	the ability of polypeptides of	disease, multiple sclerosis
	the invention (including	and/or as described below),
	antibodies and agonists or	neoplastic disorders (e.g.,
	antagonists of the invention) to	organ cancers such as lung,
	regulate production and/or	liver, colon cancer, and/or as
	secretion of IL-8 from	described below under
	endothelial cells (such as	"Hyperproliferative
	human umbilical vein	Disorders"), and
	endothelial cells (HUVEC)).	cardiovascular disorders (e.g.
	HUVECs are endothelial cells	such as described below under
	which line venous blood	"Cardiovascular Disorders").
	vessels, and are involved in	Preferred indications include
	functions that include, but are	thrombosis, bacteremia and
	not limited to, angiogenesis,	sepsis syndrome and
	vascular permeability, vascular	consequent complications
	tone, and immune cell	(such as acute respiratory
	extravasation. Endothelial	distress syndrome and
	cells play a pivotal role in the	systemic ischemia-reperfusion
	initiation and perpetuation of	resulting from septic shock),
	inflammation and secretion of	restnosis and atherosclerosis.
	IL-8 may play an important	
	role in recruitment and	
	activation of immune cells	
	such as neutrophils,	
	macrophages, and	

				lymphocytes.	
119	HDPOE32	1067	Production of	Assays for measuring expression of ICAM-1 are	Preferred embodiments of the invention include using
}				well-known in the art and may	polypeptides of the invention
				be used or routinely modified	(or antibodies, agonists, or
				to assess the ability of	antagonists thereof) in
				polypeptides of the invention	detection, diagnosis,
				(including antibodies and	prevention, and/or treatment of
				agonists or antagonists of the	Inflammation, Vascular
				invention) to regulate ICAM-1	Disease, Athereosclerosis,
				expression. Exemplary assays	Restenosis, and Stroke
				that may be used or routinely	
				modified to measure ICAM-1	
				expression include assays	
				disclosed in: Takacs P, et al,	
				FASEB J, 15(2):279-281	
· ·				(2001); and, Miyamoto K, et	
				al., Am J Pathol, 156(5):1733-	
				1739 (2000), the contents of	
				each of which is herein	
				incorporated by reference in its	
·				entirety. Cells that may be	
				used according to these assays	
				are publicly available (e.g.,	
				through the ATCC) and/or	
				may be routinely generated.	
				Exemplary cells that may be	
				used according to these assays	
				include microvascular	
				endothelial cells (MVEC).	
	НДРОН06	1068	Production of	Assays for measuring	Preferred embodiments of the

120			ICAM-1	expression of ICAM-1 are	invention include using
				well-known in the art and may	polypeptides of the Invention
				to assess the ability of	antagonists thereof) in
				polypeptides of the invention	detection, diagnosis,
				including antibodies and	prevention, and/or treatment of
				agonists or antagonists of the	Inflammation, Vascular
				invention) to regulate ICAM-1	Disease, Athereosclerosis,
	···			expression. Exemplary assays	Restenosis, and Stroke
				that may be used or routinely	
				modified to measure ICAM-1	
				expression include assays	
				disclosed in: Takacs P, et al,	
				FASEB J, 15(2):279-281	
				(2001); and, Miyamoto K, et	
				al., Am J Pathol, 156(5):1733-	
				1739 (2000), the contents of	
				each of which is herein	
				incorporated by reference in its	
				entirety. Cells that may be	
				used according to these assays	
				are publicly available (e.g.,	
				through the ATCC) and/or	
	, .			may be routinely generated.	
				Exemplary cells that may be	
				used according to these assays	
				include microvascular	
				endothelial cells (MVEC).	
	90НОДОН	1068	Production of IL-10	Assays for production of IL-10	Highly preferred indications
120			and activation of T-	and activation of T-cells are	include allergy and asthma.
			cells.	well known in the art and may	Additional highly preferred

mune	rders	w under	p	lers"),	e.g.,	/stemic	rohn"s	sisc	low),	.g., as	sting a T		ing a T								<u>.</u>	***************************************		-						
indications include immune	and hematopoietic disorders	(e.g., as described below under	"Immune Activity", and	"Blood-Related Disorders"),	autoimmune diseases (e.g.,	rheumatoid arthritis, systemic	lupus erythematosis, Crohn's	disease, multiple sclerosis	and/or as described below),	immunodeficiencies (e.g., as	described below), boosting a T	cell-mediated immune	response, and suppressing a T	cell-mediated immune	response.															
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be used or routinely modified	to assess the ability of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) to stimulate or	inhibit production of IL-10	and/or activation of T-cells.	Exemplary assays that may be	used or routinely modified to	assess the ability of	polypeptides and antibodies of	the invention (including	agonists or antagonists of the	invention) to modulate IL-10	production and/or T-cell	proliferation include, for	example, assays such as	disclosed and/or cited in:	Robinson, DS, et al., "Th-2	cytokines in allergic disease"	Br Med Bull; 56 (4): 956-968	(2000), and Cohn, et al., "T-	helper type 2 cell-directed	therapy for asthma"	Pharmacology & Therapeutics;	88: 187-196 (2000); the	contents of each of which are	herein incorporated by	reference in their entirety.	Exemplary cells that may be
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	Preferred embodiments of the invention include using polypeptides of the invention (or antibodies, agonists, or antagonists thereof) in detection, diagnosis, prevention, and/or treatment of Cancer, Wound Healing, and Inflamation. Highly preferred indications include neoplastic diseases (e.g., as described below under "Hyperproliferative"
used according to these assays include Th2 cells. IL10 secreted from Th2 cells may be measured as a marker of Th2 cell activation. Th2 cells are a class of T cells that secrete IL4, IL10, IL13, IL5 and IL6. Factors that induce differentiation and activation of Th2 cells play a major role in the initiation and pathogenesis of allergy and asthma. Primary T helper 2 cells are generated via in vitro culture under Th2 polarizing conditions using peripheral blood lymphocytes isolated from cord blood.	Assays for the activation of transcription through the Gamma Interferon Activation Site (GAS) response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate STAT transcription factors and modulate gene expression
	Activation of transcription through GAS response element in epithelial cells (such as HELA cells).
	1069
	HDP0Z56
	121

Disorders"). Highly preferred	indications include neoplasms	and cancers, such as, tor	example, melanoma, and	prostate, breast, lung, colon,	pancreatic, esophageal,	stomach, brain, liver and	urinary cancer. Other preferred	indications include benign	dysproliferative disorders and	pre-neoplastic conditions, such	as, for example, hyperplasia,	metaplasia, and/or dysplasia.	Preferred indications include	include inflammation and	inflammatory disorders.															
involved in a wide variety of	cell functions. Exemplary	assays for transcription	through the GAS response	element that may be used or	routinely modified to test	GAS-response element activity	of polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) include assays	disclosed in: You M, et al, J	Biol Chem, 272(37):23376-	23381(1997); Min W, et al.,	Circ Res, 83(8):815-823	(1998); Berger et al., Gene	66:1-10 (1998); Cullen and	Malm, Methods in Enzymol	216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA	85:6342-6346 (1988);	Matikainen et al., Blood	93(6):1980-1991 (1999); and	Henttinen et al., J Immunol	155(10):4582-4587 (1995), the	contents of each of which are	herein incorporated by	reference in its entirety.	Epithelial cells that may be	used according to these assays	are publicly available (e.g.,
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(1999); Kyriakis JM, Biochem Soc Symp 64:29-48 (1999);
Chang and Karin, Nature 410(6824):37-40 (2001); and
Cobb MH, Prog Biophys Mol   Biol 71(3-4):479-500 (1999);
the contents of each of which
are herein incorporated by
reference in its entirety.
Endothelial cells that may be
used according to these assays
are publicly available (e.g.,
through the ATCC)
Exemplary endothelial cells
that may be used according to
these assays include human
umbilical vein endothelial cells
(HUVEC), which are
endothelial cells which line
venous blood vessels, and are
involved in functions that
include, but are not limited to,
angiogenesis, vascular
permeability, vascular tone,
and immune cell extravasation.

"Hyperproliferative Disorders") and disorders of	the cardiovascular system	(e.g., heart disease, congestive	heart failure, hypertension,	aortic stenosis,	cardiomyopathy, valvular	regurgitation, left ventricular	dysfunction, atherosclerosis	and atherosclerotic vascular	disease, diabetic nephropathy,	intracardiac shunt, cardiac	hypertrophy, myocardial	infarction, chronic	hemodynamic overload, and/or	as described below under	"Cardiovascular Disorders").	Highly preferred indications	include cardiovascular,	endothelial and/or angiogenic	disorders (e.g., systemic	disorders that affect vessels	such as diabetes mellitus, as	well as diseases of the vessels	themselves, such as of the	arteries, capillaries, veins	and/or lymphatics). Highly	preferred are indications that	stimulate angiogenesis and/or	cardiovascularization. Highly	preferred are indications that
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		cardiovascularization
		Highly professed indications
	-	riiginiy preferieu mucanons
		include antiangiogenic activity
		to treat solid tumors,
		leukemias, and Kaposi"s
		sarcoma, and retinal disorders.
		Highly preferred indications
		include neoplasms and cancer,
		such as, Kaposi"s sarcoma,
		hemangioma (capillary and
		cavernous), glomus tumors,
		telangiectasia, bacillary
		angiomatosis,
		hemangioendothelioma,
		angiosarcoma,
		haemangiopericytoma,
		lymphangioma,
		lymphangiosarcoma. Highly
		preferred indications also
		include cancers such as,
		prostate, breast, lung, colon,
		pancreatic, esophageal,
		stomach, brain, liver, and
		urinary cancer. Preferred
		indications include benign
		dysproliferative disorders and
		pre-neoplastic conditions, such
		as, for example, hyperplasia,
		metaplasia, and/or dysplasia.
		Highly preferred indications

also include arterial disease, such as, atherosclerosis,	hypertension, coronary artery	disease, inflammatory	vasculitides, Reynaud"s	disease and Reynaud"s	phenomenom, aneurysms,	restenosis; venous and	lymphatic disorders such as	thrombophlebitis,	lymphangitis, and	lymphedema; and other	vascular disorders such as	peripheral vascular disease,	and cancer. Highly	preferred indications also	include trauma such as	wounds, burns, and injured	tissue (e.g., vascular injury	such as, injury resulting from	balloon angioplasty, and	atheroschlerotic lesions),	implant fixation, scarring,	ischemia reperfusion injury,	rheumatoid arthritis,	cerebrovascular disease, renal	diseases such as acute renal	failure, and osteoporosis.	Additional highly preferred	indications include stroke,	graft rejection, diabetic or
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other retinopathies, thrombotic	and coagulative disorders,	vascularitis, lymph	angiogenesis, sexual disorders,	age-related macular	degeneration, and treatment	/prevention of endometriosis	and related conditions.	Additional highly preferred	indications include fibromas,	heart disease, cardiac arrest,	heart valve disease, and	vascular disease.	Preferred indications include	blood disorders (e.g., as	described below under	"Immune Activity", "Blood-	Related Disorders", and/or	"Cardiovascular Disorders").	Preferred indications include	autoimmune diseases (e.g.,	rheumatoid arthritis, systemic	lupus erythematosis, multiple	sclerosis and/or as described	below) and	immunodeficiencies (e.g., as	described below). Additional	preferred indications include	inflammation and	inflammatory disorders (such	as acute and chronic
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inflammatory diseases, e.g., inflammatory bowel disease and Crohn's disease), and pain management.	A highly preferred embodiment of the invention includes a method for stimulating endothelial cell growth. An alternative highly preferred embodiment of the invention includes a method for inhibiting endothelial cell growth. A highly preferred embodiment of the invention includes a method for stimulating endothelial cell proliferation. An alternative highly preferred embodiment of the invention includes a method for inhibiting endothelial cell proliferation. A highly preferred embodiment of the invention includes a method for stimulating apoptosis of endothelial cells. An alternative highly preferred embodiment of the invention includes a method for inhibiting apoptosis of endothelial cells. An alternative highly preferred embodiment of the invention includes a method for inhibiting apoptosis of endothelial cells. An
	Kinase assay. JNK kinase assays for signal transduction that regulate cell proliferation, activation, or apoptosis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention, activation, and apoptosis. Exemplary assays for JNK kinase activity that may be used or routinely modified to test JNK kinase-induced activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include the assays disclosed in Forrer et al., Biol Chem 379(8-9):1101-1110 (1998); Gupta et al., Exp Cell Res 247(2): 495-504 (1999); Kyriakis JM, Biochem Soc. Symp 64:29-48 (1999).
	Activation of Endothelial Cell JNK Signaling Pathway.
	1070
	HDPSP54
	122

highly preferred embodiment of the invention includes a method for stimulating endothelial cell activation. An alternative highly preferred embodiment of the invention	includes a method for inhibiting the activation of and/or inactivating endothelial cells. A highly preferred embodiment of the invention includes a method for	stimulating angiogenisis. An alternative highly preferred embodiment of the invention includes a method for inhibiting angiogenesis. A highly preferred embodiment of the invention includes a method for reducing cardiac	
Chang and Karin, Nature 410(6824):37-40 (2001); and Cobb MH, Prog Biophys Mol Biol 71(3-4):479-500 (1999); the contents of each of which	are herein incorporated by reference in its entirety. Endothelial cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary endothelial cells	that may be used according to these assays include human umbilical vein endothelial cells (HUVEC), which are endothelial cells which line venous blood vessels, and are involved in functions that	include, but are not ilmited to, angiogenesis, vascular permeability, vascular tone, and immune cell extravasation.

disease, inflammatory	vascullindes, Keynaud's	disease and Keynaud s	phenomenom, aneurysms,	restenosis; venous and	lymphatic disorders such as	thrombophlebitis,	lymphangitis, and	lymphedema; and other	vascular disorders such as	peripheral vascular disease,	and cancer. Highly	preferred indications also	include trauma such as	wounds, burns, and injured	tissue (e.g., vascular injury	such as, injury resulting from	balloon angioplasty, and	atheroschlerotic lesions),	implant fixation, scarring,	ischemia reperfusion injury,	rheumatoid arthritis,	cerebrovascular disease, renal	diseases such as acute renal	failure, and osteoporosis.	Additional highly preferred	indications include stroke,	graft rejection, diabetic or	other retinopathies, thrombotic	and coagulative disorders,	vascularitis, lymph
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angiogenesis, sexual disorders,	age-related macular	degeneration, and treatment	/prevention of endometriosis	and related conditions.	Additional highly preferred	indications include fibromas,	heart disease, cardiac arrest,	heart valve disease, and	vascular disease.	Preferred indications include	blood disorders (e.g., as	described below under	"Immune Activity", "Blood-	Related Disorders", and/or	"Cardiovascular Disorders").	Preferred indications include	autoimmune diseases (e.g.,	rheumatoid arthritis, systemic	lupus erythematosis, multiple	sclerosis and/or as described	below) and	immunodeficiencies (e.g., as	described below). Additional	preferred indications include	inflammation and	inflammatory disorders (such	as acute and chronic	inflammatory diseases, e.g.,	inflammatory bowel disease	and Crohn's disease), and pain
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122	HDDCDCA				•
122		1070	Regulation of	Caspase Apoptosis. Assays	A highly preferred
			apoptosis in	for caspase apoptosis are well	indication is diabetes mellitus.
			pancreatic beta	known in the art and may be	An additional highly preferred
			cells.	used or routinely modified to	indication is a complication
				assess the ability of	associated with diabetes (e.g.,
				polypeptides of the invention	diabetic retinopathy, diabetic
				(including antibodies and	nephropathy, kidney disease
				agonists or antagonists of the	(e.g., renal failure,
				invention) to promote caspase	nephropathy and/or other
				protease-mediated apoptosis.	diseases and disorders as
				Apoptosis in pancreatic beta is	described in the "Renal
				associated with induction and	Disorders" section below),
-				progression of diabetes.	diabetic neuropathy, nerve
				Exemplary assays for caspase	disease and nerve damage
				apoptosis that may be used or	(e.g., due to diabetic
				routinely modified to test	neuropathy), blood vessel
				capase apoptosis activity of	blockage, heart disease, stroke,
				polypeptides of the invention	impotence (e.g., due to diabetic
				(including antibodies and	neuropathy or blood vessel
				agonists or antagonists of the	blockage), seizures, mental
				invention) include the assays	confusion, drowsiness,
				disclosed in: Loweth, AC, et	nonketotic hyperglycemic-
				al., FEBS Lett, 400(3):285-8	hyperosmolar coma,
				(1997); Saini, KS, et al.,	cardiovascular disease (e.g.,
				Biochem Mol Biol Int,	heart disease, atherosclerosis,
				39(6):1229-36 (1996);	microvascular disease,
				Krautheim, A., et al., Br J	hypertension, stroke, and other
				Pharmacol, 129(4):687-94	diseases and disorders as
				(2000); Chandra J, et al.,	described in the
				Diabetes, 50 Suppl 1:S44-7	"Cardiovascular Disorders"

		(2001); Suk K, et al., J Immunol, 166(7):4481-9 (2001); Tejedo J, et al., FEBS Lett, 459(2):238-43 (1999); Zhang, S., et al., FEBS Lett, 455(3):315-20 (1999); Lee et al., FEBS Lett 485(2-3): 122-126 (2000); Nor et al., J Vasc Res 37(3): 209-218 (2000); and Karsan and Harlan, J Atheroscler Thromb 3(2): 75-80 (1996); the contents of each of which are herein incorporated by reference in its entirety. Pancreatic cells that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary pancreatic cells that may be used according to these assays include RIN-m. RIN-m is a rat adherent pancreatic beta cell insulinoma cell line derived from a radiation	section below), dyslipidemia, endocrine disorders (as described in the "Endocrine Disorders" section below), neuropathy, vision impairment (e.g., diabetic retinopathy and blindness), ulcers and impaired wound healing, and infection (e.g., infectious diseases and disorders as described in the "Infectious Diseases" section below, especially of the urinary tract and skin), carpal tunnel syndrome and Dupuytren's contracture). An additional highly preferred indications associated with obesity. Additional highly preferred indications include weight loss or alternatively, weight gain. Aditional highly preferred indications are complications associated with insulin resistance.	
		induced transplantable rat islet cell tumor. The cells produce and secrete islet polypeptide hormones, and produce insulin,		
	-	vomstostatin and noscibly		

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	A highly preferred embodiment of the invention includes a method for stimulating the production of IFNg. An alternative highly
helper type 2 cell-directed therapy for asthma" Pharmacology & Therapeutics; 88: 187-196 (2000); the contents of each of which are herein incorporated by reference in their entirety. Exemplary cells that may be used according to these assays include Th2 cells. IL 10 secreted from Th2 cells may be measured as a marker of Th2 cell activation. Th2 cells are a class of T cells that secrete IL 4, IL 10, IL 13, IL 5 and IL 6. Factors that induce differentiation and activation of Th2 cells play a major role in the initiation and asthma. Primary T helper 2 cells are generated via in vitro culture under Th2 polarizing conditions using peripheral blood lymphocytes isolated from cord blood.	IFNgamma FMAT. IFNg plays a central role in the immune system and is considered to be a proinflammatory cytokine. IFNg promotes TH1 and
	Production of IFNgamma using a T cells
	1072
	HDPTK41
	124

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preferred embodiment of the	invention includes a method	DITID	IFNg. Highly preferred	indications include blood	disorders (e.g., as described	below under "Immune	Activity", "Blood-Related	Disorders", and/or	"Cardiovascular Disorders"),	and infection (e.g., viral	infections, tuberculosis,	infections associated with	chronic granulomatosus	disease and malignant	osteoporosis, and/or as	described below under	"Infectious Disease"). Highly	preferred indications include	autoimmune disease (e.g.,	rheumatoid arthritis, systemic	lupus erythematosis, multiple	sclerosis and/or as described	below), immunodeficiency	(e.g., as described below),	boosting a T cell-mediated	immune response, and	suppressing a T cell-mediated	immune response. Additional	highly preferred indications	include inflammation and
inhibits TH2 differentiation;	promotes 1gG2a and inhibits	lgE secretion; induces	macrophage activation; and	increases MHC expression.	Assays for immunomodulatory	proteins produced by T cells	and NK cells that regulate a	variety of inflammatory	activities and inhibit TH2	helper cell functions are well	known in the art and may be	used or routinely modified to	assess the ability of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) to mediate	immunomodulation, regulate	inflammatory activities,	modulate TH2 helper cell	function, and/or mediate	humoral or cell-mediated	immunity. Exemplary assays	that test for	immunomodulatory proteins	evaluate the production of	cytokines, such as Interferon	gamma (IFNg), and the	activation of T cells. Such	assays that may be used or
		-																	-			-					-			

7.1	routinely modified to test	inflammatory disorders.
 <u></u>	immunomodulatory activity of	Additional preferred
d	polypeptides of the invention	indications include idiopathic
<u> </u>	(including antibodies and	pulmonary fibrosis. Highly
 <u> </u>	agonists or antagonists of the	preferred indications include
 ii	invention) include the assays	neoplastic diseases (e.g.,
<del>p</del>	disclosed in Miraglia et al., J	leukemia, lymphoma,
<u> </u>	Biomolecular Screening 4:193-	melanoma, and/or as described
2	204 (1999); Rowland et al.,	below under
<u></u>	"Lymphocytes: a practical	"Hyperproliferative
<u> </u>	approach" Chapter 6:138-160	Disorders"). Highly preferred
	(2000); Gonzalez et al., J Clin	indications include neoplasms
	Lab Anal 8(5):225-233 (1995);	and cancers, such as, for
 <u> </u>	Billiau et al., Ann NY Acad	example, leukemia, lymphoma,
8	Sci 856:22-32 (1998); Boehm	melanoma, and prostate,
0	et al., Annu Rev Immunol	breast, lung, colon, pancreatic,
	15:749-795 (1997), and	esophageal, stomach, brain,
	Rheumatology (Oxford)	liver and urinary cancer. Other
	38(3):214-20 (1999), the	preferred indications include
-	contents of each of which are	benign dysproliferative
 ų	herein incorporated by	disorders and pre-neoplastic
7.	reference in its entirety.	conditions, such as, for
<u> </u>	Human T cells that may be	example, hyperplasia,
n	used according to these assays	metaplasia, and/or dysplasia.
u	may be isolated using	Preferred indications include
te	techniques disclosed herein or	anemia, pancytopenia,
0	otherwise known in the art.	leukopenia, thrombocytopenia,
H	Human T cells are primary	Hodgkin's disease, acute
H H	human lymphocytes that	lymphocytic anemia (ALL),
u	mature in the thymus and	plasmacytomas, multiple
e	express a T Cell receptor and	myeloma, Burkitt's lymphoma,

			3	fra atimus lating (a a
		<u> </u>	and agonists or antagonists of	lor summannig (c.g.,
		4	the invention) include the	increasing) adipocyte
		<u>ਲ</u>	assays disclosed in Forrer et	activation. An alternative
		[a]	al., Biol Chem 379(8-9):1101-	highly preferred embodiment
			1110 (1998); Le Marchand-	of the invention includes a
		<u>B</u>	Brustel Y, Exp Clin	method for inhibiting the
		TI.	Endocrinol Diabetes	activation of (e.g., decreasing)
			107(2):126-132 (1999);	and/or inactivating adipocytes.
			Kyriakis JM, Biochem Soc	Highly preferred indications
		<u>S</u>	Symp 64:29-48 (1999); Chang	include endocrine disorders
			and Karin, Nature	(e.g., as described below under
		4	410(6824):37-40 (2001); and	"Endocrine Disorders").
		0	Cobb MH, Prog Biophys Mol	Highly preferred indications
		<u> </u>	Biol 71(3-4):479-500 (1999);	also include neoplastic
			the contents of each of which	diseases (e.g., lipomas,
		<u>a</u>	are herein incorporated by	liposarcomas, and/or as
			reference in its entirety.	described below under
	,		Mouse adipocyte cells that	"Hyperproliferative
		u	may be used according to these	Disorders"). Preferred
		g	assays are publicly available	indications include blood
			(e.g., through the ATCC).	disorders (e.g., hypertension,
		· 114	Exemplary mouse adipocyte	congestive heart failure, blood
		3	cells that may be used	vessel blockage, heart disease,
		8	according to these assays	stroke, impotence and/or as
		•••	include 3T3-L1 cells. 3T3-L1	described below under
		•=	is an adherent mouse	"Immune Activity",
			preadipocyte cell line that is a	"Cardiovascular Disorders",
A 444			continuous substrain of 3T3	and/or "Blood-Related
		<u> </u>	fibroblast cells developed	Disorders"), immune disorders
			through clonal isolation and	(e.g., as described below under
			undergo a pre-adipocyte to	"Immune Activity"), neural

disorders (e.g., as described below under "Neural Activity and Neurological Diseases"),	and infection (e.g., as	"Infectious Disease").	A highly preferred indication	is diabetes mellitus.	additional highly preferred	indication is a complication	associated with diabetes (e.g.,	diabetic retinopathy, diabetic	nephropathy, kidney disease	(e.g., renal failure,	nephropathy and/or other	diseases and disorders as	described in the "Renal	Disorders" section below),	diabetic neuropathy, nerve	disease and nerve damage	(e.g., due to diabetic	neuropathy), blood vessel	blockage, heart disease, stroke,	impotence (e.g., due to diabetic	neuropathy or blood vessel	blockage), seizures, mental	confusion, drowsiness,	nonketotic hyperglycemic-	hyperosmolar coma,	cardiovascular disease (e.g.,	heart disease, atherosclerosis,
adipose-like conversion under appropriate differentiation conditions known in the art.																							-				
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	·																										

microvascular disease, hypertension, stroke, and other diseases and disorders as described in the "Cardiovascular Disorders"	section below), dyslipidemia, endocrine disorders (as described in the "Endocrine Disorders" section below),	(e.g., diabetic retinopathy and blindness), ulcers and impaired wound healing, infection (e.g., infectious diseases and	disorders as described in the "Infectious Diseases" section below (particularly of the urinary tract and skin). An additional highly preferred indication is obesity and/or	complications associated with obesity. Additional highly preferred indications include weight loss or alternatively, weight gain. Additional highly preferred indications are complications associated with insulin resistance.	indications are disorders of the musculoskeletal systems
				,	

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					including myopatmes,
					muscular dystrophy, and/or as
					described herein.
					Additional highly preferred
	-				indications include,
					hypertension, coronary artery
					disease, dyslipidemia.
					gallstones, osteoarthritis.
					degenerative arthritis. eating
					disorders, fibrosis, cachexia,
					and kidney diseases or
					disorders. Preferred
					indications include neoplasms
					and cancer, such as,
					lymphoma, leukemia and
					breast, colon, and kidney
					cancer. Additional preferred
					indications include melanoma,
					prostate, lung, pancreatic,
					esophageal, stomach, brain,
					liver, and urinary cancer.
					Highly preferred indications
					include lipomas and
					liposarcomas. Other preferred
					indications include benign
					dysproliferative disorders and
					pre-neoplastic conditions, such
	,				as, for example, hyperplasia,
					metaplasia, and/or dysplasia.
	HDPUH26	1074	Inhibition of	Reporter Assay: construct	
126			squalene synthetase	contains regulatory and coding	

		A highly preferred embodiment of the invention includes a method for stimulating adipocyte proliferation. An alternative highly preferred embodiment of the invention includes a method for inhibiting adipocyte proliferation. A highly preferred embodiment of the invention includes a method for stimulating
sequence of squalene synthetase, the first specific enzyme in the cholesterol biosynthetic pathway. See Jiang, et al., J. Biol. Chem. 268:12818-128241(993), the contents of which are herein incorporated by reference in its entirety. Cells were treated with SID superparants and	SEAP activity was measured after 72 hours. HepG2 is a human hepatocellular carcinoma cell line (ATCC HB-8065). See Knowles et al., Science. 209:497-9 (1980), the contents of which are herein incorporated by reference in its	Kinase assay. Kinase assays, for example an Elk-1 kinase assay, for ERK signal transduction that regulate cell proliferation or differentiation are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote or
gene transcription.		Activation of Adipocyte ERK Signaling Pathway
		1075
		HDPUW68
		127

 ii	inhibit cell proliferation,	adipocyte differentiation. An
 8	activation, and differentiation.	alternative highly preferred
 ш	Exemplary assays for ERK	embodiment of the invention
k	kinase activity that may be	includes a method for
 n	used or routinely modified to	inhibiting adipocyte
 	test ERK kinase-induced	differentiation. A highly
 8	activity of polypeptides of the	preferred embodiment of the
 ii	invention (including antibodies	invention includes a method
 · ·	and agonists or antagonists of	for stimulating (e.g.,
 <del></del>	the invention) include the	increasing) adipocyte
 B	assays disclosed in Forrer et	activation. An alternative
 <u>a</u>	al., Biol Chem 379(8-9):1101-	highly preferred embodiment
	1110 (1998); Le Marchand-	of the invention includes a
 <u> </u>	Brustel Y, Exp Clin	method for inhibiting the
ш_	Endocrinol Diabetes	activation of (e.g., decreasing)
	107(2):126-132 (1999);	and/or inactivating adipocytes.
 <u> </u>	Kyriakis JM, Biochem Soc	Highly preferred indications
S	Symp 64:29-48 (1999); Chang	include endocrine disorders
 a	and Karin, Nature	(e.g., as described below under
 4	410(6824):37-40 (2001); and	"Endocrine Disorders").
	Cobb MH, Prog Biophys Mol	Highly preferred indications
 <u> </u>	Biol 71(3-4):479-500 (1999);	also include neoplastic
<u> </u>	the contents of each of which	diseases (e.g., lipomas,
 a	are herein incorporated by	liposarcomas, and/or as
-	reference in its entirety.	described below under
	Mouse adipocyte cells that	"Hyperproliferative
 u	may be used according to these	Disorders"). Preferred
<u>a</u>	assays are publicly available	indications include blood
 	(e.g., through the ATCC).	disorders (e.g., hypertension,
 <u> </u>	Exemplary mouse adipocyte	congestive heart failure, blood
	cells that may be used	vessel blockage, heart disease,

	according to these assays	stroke, impotence and/or as
 	include 3T3-L1 cells. 3T3-L1	described below under
 	is an adherent mouse	"Immine Activity"
 	nreadinocyte cell line that is a	"Cardiovascular Disorders"
 	continuous substrain of 3T3	and/or "Blood-Related
 	fibroblast cells developed	Disorders"), immune disorders
	through clonal isolation and	(e.g., as described below under
	undergo a pre-adipocyte to	"Immune Activity"), neural
 	adipose-like conversion under	disorders (e.g., as described
	appropriate differentiation	below under "Neural Activity
	conditions known in the art.	and Neurological Diseases"),
 		and infection (e.g., as
		described below under
 		"Infectious Disease").
 		A highly preferred indication
		is diabetes mellitus. An
 		additional highly preferred
 		indication is a complication
 		associated with diabetes (e.g.,
		diabetic retinopathy, diabetic
		nephropathy, kidney disease
 		(e.g., renal failure,
 	-	nephropathy and/or other
		diseases and disorders as
		described in the "Renal
 		Disorders" section below),
 		diabetic neuropathy, nerve
 		disease and nerve damage
 		(e.g., due to diabetic
 		neuropathy), blood vessel
		blockage, heart disease, stroke,

impotence (e.g., due to diabetic neuropathy or blood vessel	blockage), seizures, mental	confusion, drowsiness,	nonketotic hyperglycemic-	hyperosmolar coma,	cardiovascular disease (e.g.,	heart disease, atherosclerosis,	microvascular disease,	hypertension, stroke, and other	diseases and disorders as	described in the	"Cardiovascular Disorders"	section below), dyslipidemia,	endocrine disorders (as	described in the "Endocrine	Disorders" section below),	neuropathy, vision impairment	(e.g., diabetic retinopathy and	blindness), ulcers and impaired	wound healing, infection (e.g.,	infectious diseases and	disorders as described in the	"Infectious Diseases" section	below (particularly of the	urinary tract and skin). An	additional highly preferred	indication is obesity and/or	complications associated with	obesity. Additional highly	preferred indications include
																		<u>,                                      </u>											
		•							-																				

weight loss or alternatively, weight gain. Additional highly preferred indications are complications associated with insulin resistance.	Additional highly preferred indications are disorders of the musculoskeletal systems including myopathies, muscular dystrophy, and/or as	described herein. Additional highly preferred indications include, hypertension, coronary artery disease, dyslipidemia,	degenerative arthritis, eating disorders, fibrosis, cachexia, and kidney diseases or disorders. Preferred indications include neoplasms	lymphoma, leukemia and breast, colon, and kidney cancer. Additional preferred indications include melanoma, prostate, lung, pancreatic, esophageal, stomach, brain, liver, and urinary cancer.  Highly preferred indications include linomas and
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					liposarcomas. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia.
127	HDPUW68	1075	Activation of transcription through serum response element in immune cells (such as T-cells).	Assays for the activation of transcription through the Serum Response Element (SRE) are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate the serum response factors and modulate the expression of genes involved in growth. Exemplary assays for transcription through the SRE that may be used or routinely modified to test SRE activity of the polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10	A preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) TNF alpha production. An alternative preferred embodiment of the invention includes a method for stimulating (e.g., increasing) TNF alpha production. Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"), Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, Crohn"s disease, multiple sclerosis and/or as described below), immunodeficiencies
				(1998); Cullen and Malm, Methods in Enzymol 216:362-	(e.g., as described below), boosting a T cell-mediated

immune response, and	suppressing a T cell-mediated	immune response. Additional	highly preferred indications	include inflammation and	inflammatory disorders, and	treating joint damage in	patients with rheumatoid	arthritis. An additional highly	preferred indication is sepsis.	Highly preferred indications	include neoplastic diseases	(e.g., leukemia, lymphoma,	and/or as described below	under "Hyperproliferative	Disorders"). Additionally,	highly preferred indications	include neoplasms and	cancers, such as, for example,	leukemia, lymphoma,	melanoma, glioma (e.g.,	malignant glioma), solid	tumors, and prostate, breast,	lung, colon, pancreatic,	esophageal, stomach, brain,	liver and urinary cancer. Other	preferred indications include	benign dysproliferative	disorders and pre-neoplastic	conditions, such as, for	example, hyperplasia,
368 (1992); Henthorn et al.,	Proc Natl Acad Sci USA	85:6342-6346 (1988); and	Black et al., Virus Genes	12(2):105-117 (1997), the	content of each of which are	herein incorporated by	reference in its entirety. T	cells that may be used	according to these assays are	publicly available (e.g.,	through the ATCC).	Exemplary mouse T cells that	may be used according to these	assays include the CTLL cell	line, which is an IL-2	dependent suspension culture	of T cells with cytotoxic	activity.												
													-								-	-	-							
																	•												•	

					metaplasia, and/or dysplasia. Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, cardiac reperfusion injury, and asthma and allergy. An additional preferred indication is infection (e.g., an infectious disease as described below
127	HDPUW68	1075	Stimulation of Calcium Flux in pancreatic beta cells.	Assays for measuring calcium flux are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of	A highly preferred indication is diabetes mellitus. An additional highly preferred indication is a complication associated with diabetes (e.g., diabetic retinopathy, diabetic nephropathy, kidney disease

the in	the invention) to mobilize	(e.g., renal failure.
 calciu	calcium. For example, the	nephropathy and/or other
FLPR	FLPR assay may be used to	diseases and disorders as
meası	measure influx of calcium.	described in the "Renal
 Cells	Cells normally have very low	Disorders" section below),
conce	concentrations of cytosolic	diabetic neuropathy, nerve
calcir	calcium compared to much	disease and nerve damage
highe	higher extracellular calcium.	(e.g., due to diabetic
Extra	Extracellular factors can cause	neuropathy), blood vessel
 an int	an influx of calcium, leading to	blockage, heart disease, stroke,
 active	activation of calcium	impotence (e.g., due to diabetic
respo	responsive signaling pathways	neuropathy or blood vessel
 anda	and alterations in cell	blockage), seizures, mental
funct	functions. Exemplary assays	confusion, drowsiness,
that n	that may be used or routinely	nonketotic hyperglycemic-
 ipom	modified to measure calcium	hyperosmolar coma,
flux b	flux by polypeptides of the	cardiovascular disease (e.g.,
inven	invention (including antibodies	heart disease, atherosclerosis,
anda	and agonists or antagonists of	microvascular disease,
the in	the invention) include assays	hypertension, stroke, and other
discle	disclosed in: Satin LS, et al.,	diseases and disorders as
Endo	Endocrinology, 136(10):4589-	described in the
601 (	601 (1995);Mogami H, et al.,	"Cardiovascular Disorders"
Endo	Endocrinology, 136(7):2960-6	section below), dyslipidemia,
(1993	(1995); Richardson SB, et al.,	endocrine disorders (as
 Bioch	Biochem J, 288 (Pt 3):847-51	described in the "Endocrine
(1992	(1992); and, Meats, JE, et al.,	Disorders" section below),
Cell C	Cell Calcium 1989 Nov-	neuropathy, vision impairment
Dec;1	Dec;10(8):535-41 (1989), the	(e.g., diabetic retinopathy and
conte	contents of each of which is	blindness), ulcers and impaired
herei	herein incorporated by	wound healing, and infection

				reference in its entirety.	(e.g., infectious diseases and
				Pancreatic cells that may be	disorders as described in the
			-	used according to these assays	"Infectious Diseases" section
				are publicly available (e.g.,	below, especially of the
				through the ATCC) and/or	urinary tract and skin), carpal
				may be routinely generated.	tunnel syndrome and
				Exemplary pancreatic cells that	Dupuytren's contracture).
				may be used according to these	An additional highly preferred
				assays include HITT15 Cells.	indication is obesity and/or
				HITT15 are an adherent	complications associated with
				epithelial cell line established	obesity. Additional highly
				from Syrian hamster islet cells	preferred indications include
				transformed with SV40. These	weight loss or alternatively,
				cells express glucagon,	weight gain. Aditional
				somatostatin, and	highly preferred indications are
				glucocorticoid receptors. The	complications associated with
				cells secrete insulin, which is	insulin resistance.
				stimulated by glucose and	
				glucagon and suppressed by	
				somatostatin or	
				glucocorticoids. ATTC# CRL-	
				1777 Refs: Lord and	
				Ashcroft. Biochem. J. 219:	
				547-551; Santerre et al. Proc.	
				Natl. Acad. Sci. USA 78:	
				4339-4343, 1981.	
	HDPUW68	1075	Activation of	Kinase assay. Kinase assays,	A highly preferred
127			Skeletal Mucle Cell	for example an GSK-3 kinase	embodiment of the invention
			PI3 Kinase	assay, for PI3 kinase signal	includes a method for
			Signalling Pathway	transduction that regulate	increasing muscle cell survival
		3		glucose metabolism and cell	An alternative highly preferred

	survivial are well-known in the	embodiment of the invention
	 art and may be used or	includes a method for
	 routinely modified to assess	decreasing muscle cell
	the ability of polypeptides of	survival. A preferred
	 the invention (including	embodiment of the invention
	 antibodies and agonists or	includes a method for
	 antagonists of the invention) to	stimulating muscle cell
	 promote or inhibit glucose	proliferation. In a specific
	metabolism and cell survival.	embodiment, skeletal muscle
	 Exemplary assays for PI3	cell proliferation is stimulated.
	kinase activity that may be	An alternative highly preferred
	 used or routinely modified to	embodiment of the invention
	test PI3 kinase-induced activity	includes a method for
	 of polypeptides of the	inhibiting muscle cell
	invention (including antibodies	proliferation. In a specific
	and agonists or antagonists of	embodiment, skeletal muscle
	the invention) include assays	cell proliferation is inhibited.
	 disclosed in Forrer et al., Biol	A preferred embodiment of
	 Chem 379(8-9):1101-1110	the invention includes a
	 (1998); Nikoulina et al.,	method for stimulating muscle
	Diabetes 49(2):263-271	cell differentiation. In a
	 (2000); and Schreyer et al.,	specific embodiment, skeletal
	Diabetes 48(8):1662-1666	muscle cell differentiation is
	 (1999), the contents of each of	stimulated. An alternative
	 which are herein incorporated	highly preferred embodiment
	by reference in its entirety.	of the invention includes a
	 Rat myoblast cells that may be	method for inhibiting muscle
	 used according to these assays	cell differentiation. In a
	 are publicly available (e.g.,	specific embodiment, skeletal
	 through the ATCC).	muscle cell differentiation is
-	Exemplary rat myoblast cells	inhibited. Highly preferred

indications include disorders of the musculoskeletal system. Preferred indications include	neoplastic diseases (e.g., as described below under "Hyperproliferative"	Disorders"), endocrine disorders (e.g., as described below under "Endocrine	Disorders"), neural disorders (e.g., as described below under	Neurological Diseases"), blood	disorders (e.g., as described	Activity", "Cardiovascular	Disorders", and/or "Blood-	Related Disorders"), immune	disorders (e.g., as described	Activity"), and infection (e.g.,	as described below under	"Infectious Disease"). A	highly preferred indication is	diabetes mellitus.	additional highly preferred	indication is a complication	associated with diabetes (e.g.,	diabetic retinopathy, diabetic	nephropathy, kidney disease	(e.g., renal failure,
that may be used according to these assays include L6 cells. L6 is an adherent rat myoblast	cell line, isolated from primary cultures of rat thigh muscle, that fuses to form	multinucleated myotubes and striated fibers after culture in differentiation media.		47																
												•								-
												-		-			•••			

			nephropathy and/or other
			diseases and disorders as
			described in the "Renal
			Disorders" section below),
			diabetic neuropathy, nerve
 			disease and nerve damage (e.g.,
 		-	due to diabetic neuropathy),
			blood vessel blockage, heart
			disease, stroke, impotence
			(e.g., due to diabetic
 			neuropathy or blood vessel
 			blockage), seizures, mental
			confusion, drowsiness,
 			nonketotic hyperglycemic-
•••			hyperosmolar coma,
 			cardiovascular disease (e.g.,
 			heart disease, atherosclerosis,
 λ			microvascular disease,
 			hypertension, stroke, and other
 			diseases and disorders as
			described in the
			"Cardiovascular Disorders"
			section below), dyslipidemia,
			endocrine disorders (as
 			described in the "Endocrine
 			Disorders" section below),
 -			neuropathy, vision impairment
 			(e.g., diabetic retinopathy and
 			blindness), ulcers and impaired
	٠		wound healing, infections
			(e.g., infectious diseases and

disorders as described in the	"Intectious Diseases" section	below, especially of the	urinary tract and skin), carpal	tunnel syndrome and	Dupuytren's contracture).	An additional highly preferred	indication is obesity and/or	complications associated with	obesity. Additional highly	preferred indications include	weight loss or alternatively,	weight gain. Additional	highly preferred indications are	complications associated with	insulin resistance.	Additonal highly preferred	indications are disorders of the	musculoskeletal system	including myopathies,	muscular dystrophy, and/or as	described herein.	Additional highly preferred	indications include: myopathy,	atrophy, congestive heart	failure, cachexia, myxomas,	fibromas, congenital	cardiovascular abnormalities,	heart disease, cardiac arrest,	heart valve disease, and	vascular disease Highly
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preferred indications include neoplasms and cancer, such as, rhabdomyoma, rhabdosarcoma, stomach, esophageal, prostate, and urinary cancer. Preferred indications also include breast, lung, colon, pancreatic, brain, and liver cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, hyperplasia, metaplasia, and/or dysplasia.	Highly preferred indications include inflammation and inflammatory disorders. Highly preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"). Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below), and immunodeficiencies (e.g., as
ne cs. in	Assays for the activation of transcription through the in NFKB response element are well-known in the art and may be used or routinely modified in to assess the ability of as polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate NFKB Hranscription factors and modulate expression of immunomodulatory genes. Exemplary assays for transcription through the delay.
	Activation of transcription transcription transcription transcription NFKB Neesponse element in we immune cells (such as T-cells).
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	НДРУН60
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	may be used or rountinely	described below). An
	modified to test NFKB-	additional highly preferred
	response element activity of	indication is infection (e.g.,
	 polypeptides of the invention	AIDS, and/or an infectious
	including antibodies and	disease as described below
	agonists or antagonists of the	under "Infectious Disease").
	invention) include assays	Highly preferred indications
	disclosed in Berger et al., Gene	include neoplastic diseases
	66:1-10 (1998); Cullen and	(e.g., melanoma, leukemia,
	Malm, Methods in Enzymol	lymphoma, and/or as described
	216:362-368 (1992); Henthorn	below under
	et al., Proc Natl Acad Sci USA	"Hyperproliferative
	 85:6342-6346 (1988); Black et	Disorders"). Highly preferred
	al., Virus Gnes 15(2):105-117	indications include neoplasms
	(1997); and Fraser et al.,	and cancers, such
	 29(3):838-844 (1999), the	as,melanoma, renal cell
	contents of each of which are	carcinoma, leukemia,
	herein incorporated by	lymphoma, and prostate,
	reference in its entirety. T	breast, lung, colon, pancreatic,
	cells that may be used	esophageal, stomach, brain,
	according to these assays are	liver and urinary cancer. Other
	publicly available (e.g.,	preferred indications include
	through the ATCC).	benign dysproliferative
	Exemplary human T cells that	disorders and pre-neoplastic
	may be used according to these	conditions, such as, for
	assays include the SUPT cell	example, hyperplasia,
	line, which is a suspension	metaplasia, and/or dysplasia.
	 culture of IL-2 and IL-4	Preferred indications also
	responsive T cells.	include anemia, pancytopenia,
		leukopenia, thrombocytopenia,
		Hodgkin's disease, acute

lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, suppression of immune reactions to transplanted organs, asthma and allergy.	Highly preferred indications include allergy, asthma, and rhinitis. Additional preferred indications include infection (e.g., an infectious disease as described below under "Infectious Disease"), and inflammation and inflammatory disorders. Preferred indications also include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"). Preferred indications include autoimmune diseases (e.g.,
	This reporter assay measures activation of the GATA-3 signaling pathway in HMC-1 human mast cell line. Activation of GATA-3 in mast cells has been linked to cytokine and chemokine production. Assays for the activation of transcription through the GATA3 response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to
	Activation of transcription through GATA-3 response element in immune cells (such as mast cells).
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remilate GATA3 transcription	rheumatoid arthritis, systemic
factors and modulate	lunus ervthematosis, multiple
	alpha of functional or described
expression of mast cell genes	Scierosis aliu/oi as described
important for immune response	below) and
development. Exemplary	immunodeficiencies (e.g., as
assays for transcription	described below). Preferred
through the GATA3 response	indications include neoplastic
element that may be used or	diseases (e.g., leukemia,
routinely modified to test	lymphoma, melanoma,
GATA3-response element	prostate, breast, lung, colon,
activity of polypeptides of the	pancreatic, esophageal,
invention (including antibodies	stomach, brain, liver, and
and agonists or antagonists of	urinary tract cancers and/or as
 the invention) include assays	described below under
disclosed in Berger et al., Gene	"Hyperproliferative
66:1-10 (1998); Cullen and	Disorders"). Other preferred
Malm, Methods in Enzymol	indications include benign
216:362-368 (1992); Henthorn	dysproliferative disorders and
et al., Proc Natl Acad Sci USA	pre-neoplastic conditions, such
85:6342-6346 (1988); Flavell	as, for example, hyperplasia,
et al., Cold Spring Harb Symp	metaplasia, and/or dysplasia.
Quant Biol 64:563-571 (1999);	Preferred indications include
Rodriguez-Palmero et al., Eur	anemia, pancytopenia,
J Immunol 29(12):3914-3924	leukopenia, thrombocytopenia,
 (1999); Zheng and Flavell,	leukemias, Hodgkin's disease,
Cell 89(4):587-596 (1997); and	acute lymphocytic anemia
Henderson et al., Mol Cell Biol	(ALL), plasmacytomas,
14(6):4286-4294 (1994), the	multiple myeloma, Burkitt's
contents of each of which are	lymphoma, arthritis, AIDS,
herein incorporated by	granulomatous disease,
reference in its entirety. Mast	inflammatory bowel disease,

sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, and Lyme Disease.	
cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary human mast cells that may be used according to these assays include the HMC-1 cell line, which is an immature human mast cell line established from the peripheral blood of a patient with mast cell leukemia, and exhibits many characteristics of immature mast cells.	Assays for the regulation (i.e. increases or decreases) of viability and proliferation of cells in vitro are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate viability and proliferation of pre-adipose cells and cell lines. For example, the CellTiter-Gloô Luminescent Cell Viability Assay (Promega Corp., Madison, WI, USA) can be
	Proliferation of preadipose cells (such as 3T3-L1 cells)
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	Highly preferred indications include asthma, allergy, hypersensitivity reactions, inflammation, and inflammatory disorders.  Additional highly preferred indications include immune and hematopoietic disorders (e.g., as described below under "Immune Activity", and "Blood-Related Disorders"), autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, Crohn"s
used to measure the number of viable cells in culture based on quantitation of the ATP present which signals the present of metabolically active cells. 3T3-L1 is a mouse preadipocyte cell line. It is a continuous substrain of 3T3 fibroblast cells developed through clonal isolation. Cells were differentiated to an adipose-like state before being used in the screen. See Green H and Meuth M., Cell 3: 127-133 (1974), which is herein incorporated by reference in its entirety.	Kinase assay. JNK kinase assays for signal transduction that regulate cell proliferation, activation, or apoptosis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote or inhibit cell proliferation, activation, and apoptosis.  Exemplary assays for JNK
	Activation of JNK Signaling Pathway in immune cells (such as eosinophils).
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kinase activity that may be	disease multiple sclerosis
used or routinely modified to	and/or as described below),
test JNK kinase-induced	immunodeficiencies (e.g., as
activity of polypeptides of the	described below). Highly
invention (including antibodies	preferred indications also
and agonists or antagonists of	include boosting or inhibiting
the invention) include the	immune cell proliferation.
assays disclosed in Forrer et	Preferred indications include
al., Biol Chem 379(8-9):1101-	neoplastic diseases (e.g.,
1110 (1998); Gupta et al., Exp	leukemia, lymphoma, and/or as
Cell Res 247(2): 495-504	described below under
(1999); Kyriakis JM, Biochem	"Hyperproliferative
 Soc Symp 64:29-48 (1999);	Disorders"). Highly preferred
Chang and Karin, Nature	indications include boosting an
 410(6824):37-40 (2001); and	eosinophil-mediated immune
Cobb MH, Prog Biophys Mol	response, and suppressing an
Biol 71(3-4):479-500 (1999);	eosinophil-mediated immune
the contents of each of which	response.
are herein incorporated by	
 reference in its entirety.	
Exemplary cells that may be	
used according to these assays	
include eosinophils.	
Eosinophils are important in	
the late stage of allergic	
reactions; they are recruited to	
tissues and mediate the	
inflammatory response of late	
stage allergic reaction.	
Moreover, exemplary assays	
that may be used or routinely	

modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to modulate signal transduction, cell proliferation, activation, or apoptosis in eosinophils include assays disclosed and/or cited in: Zhang JP, et al., "Role of caspases in dexamethasone-induced apoptosis and activation of c-Jun NH2-terminal kinase and p38 mitogen-activated protein kinase in human eosinophils." Clin Exp Immunol; Oct;122(1):20-7 (2000); Hebestreit H, et al., "Disruption of fas receptor signaling by nitric oxide in eosinophils." J Exp Med; Feb 2;187(3):415-25 (1999); Allergy Clin Immunol 1999 Sep; 104(3 Pt 1):565-74; and, Sousa AR, et al., "In vivo resistance to corticosteroids in bronchial asthma is associated with enhanced phosyphorylation of July N-terminal kinase and stallure of terminal kinase and stallure of				
	modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to modulate signal transduction, cell proliferation, activation, or	apoptosis in eosinophils include assays disclosed and/or cited in: Zhang JP, et al., "Role of caspases in dexamethasone-induced apoptosis and activation of c-Jun NH2-terminal kinase and p38 mitogen-activated protein	kinase in human eosinophils" Clin Exp Immunol; Oct;122(1):20-7 (2000); Hebestreit H, et al., "Disruption of fas receptor signaling by nitric oxide in eosinophils" J Exp Med; Feb 2;187(3):415-25 (1998); J	Allergy Clin Immunol 1999 Sep;104(3 Pt 1):565-74; and, Sousa AR, et al., "In vivo resistance to corticosteroids in bronchial asthma is associated with enhanced phosyphorylation of JUN N- terminal kinase and failure of
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embodiment of the invention includes a method for inhibiting (e.g., decreasing) apoptosis of endothelial cells. A highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing)	endothelial cell activation. An alternative highly preferred embodiment of the invention includes a method for inhibiting (e.g., decreasing) the activation of and/or inactivating endothelial cells		mer s a diac tive tive mer s a diac
al., Biol Chem 379(8-9):1101-1110 (1998); Gupta et al., Exp Cell Res 247(2): 495-504 (1999); Kyriakis JM, Biochem Soc Symp 64:29-48 (1999); Chang and Karin, Nature 410(6824):37-40 (2001); and Cobb MH, Prog Biophys Mol	Biol 71(3-4):479-500 (1999); the contents of each of which are herein incorporated by reference in its entirety.  Endothelial cells that may be used according to these assays	through the ATCC). Exemplary endothelial cells that may be used according to these assays include human umbilical vein endothelial cells (HUVEC), which are endothelial cells which line venous blood vessels, and are	involved in functions that include, but are not limited to, angiogenesis, vascular permeability, vascular tone, and immune cell extravasation.

preferred indications include neoplastic diseases (e.g., sa described below under "Hyperpoliferative Disorders"), and disorders of the cardionyopath system (e.g., heart disease, congestive heart failure, hypertension, aortic stenosis, cardionyopathy, valvular regurgitation, elt ventricular dysfunction, altheroselerosis and atheroselerosis and atheroselerosic orbitopathy, intracardiae shunt, cardiac hypertrophy, myocardial infarction, chronic hemodynamic overload, and/or as described below under "Cardiovascular Disorders"). Highly preferred indications include cardiovascular Disorders"). Highly preferred indications include cardiovascular bisorders"). Highly preferred indications include cardiovascular, endotherial and/or angiogenic disorders (e.g., systemic diso	$\Gamma$										-							•											-		
preferred indications inclu  neoplastic diseases (e.g., a described below under "Hyperpoliferative Disorders"), and disorders the cardiovascular system (e.g., heart disease, conges heart failure, hypertension, aortic stenosis, cardiomyopathy, valvular regurgitation, left ventricul dysfunction, atheroselerosi and atheroselerosi and atheroselerosi and atheroselerosi intracardiac shunt, cardiac hypertrophy, myocardial infaction, chronic hemodynamic overload, an as described below under "Cardiovascular Disorders' Highly preferred indication include cardiovascular) isorders' Highly preferred indication include cardiovascular, endothelial and/or angioge disorders that affect vessel such as disbetes mellitus, e well as diseases of the vess themselves, such as of the arteries, capillaries, veins and/or lymphatics). Highly preferred are indications th	<u>و</u>				of		tive				ar	S	Ħ	hy,				ıd/oı		<u>ښ</u>	JS		nic		S	ST	sels			>	ıat
preferred indications in neoplastic diseases (e.g. described below under "Hyperproliferative Disorders"), and disord the cardiovascular syst (e.g., heart disease, con heart failure, hypertens acrtic stenois; cardiomyopathy, valvu regugitation, left ventr dysfunction, atheroselentic vas disease, diabetic nephru intracardiae shunt, card hypertophy, myocardi infarction, chronic hemodynamic overload as described below und "Cardiovascular Disord Highly preferred indic include cardiovascular disorders (e.g., systemid disorders that affect ve such as diabetes melliti well as diseases of the themselves, such as of arteries, capillaries, via and and/or lymphatics). Hyperferred are indication preferred are indication	cluc	., as			ers	m	gest	ion,		lar	icul	rosi	cula	opat	liac	a		l, an	ler.	lers	ation	. •	oge	၁	ssel	us, a	ves	the	us	llg	ıs th
preferred indication neoplastic diseases described below un "Hyperproliferative Disorders"), and dis the cardiovascular s (e.g., heart disease, heart failure, hypert aortic stenosis, cardiomyopathy, vergurgitation, eft v dysfunction, athero and atheroselectotic disease, diabeta shunt, hypertrophy, myoco infarction, chronic hemodynamic over as described boll 'Cardiovascular Dil Highly preferred in include cardiovasc endothelial and/or disorders (e.g., syst disorders that affec such as diseases of themselves, such as arteries, capillaries, preferred are indica	s in	(e.g	der		sord	yste	con	ens		lvu	entr	scle	vas	phr	card	ardi		load	pun	sorc	dica	ular	ingi	emi	t ve	alit	the	of	, vei	Ξ	ξį.
preferred indica neoplastic disea described below "Hyperprolifera Disorders"), and the cardiovascu (e.g., heart discinue, by acrtic stenosis, cardiomyopathy, regurgitation, led dysfunction, att and atheroscleri disease, diabetti intracardiae shub hypertrophy, minfarction, chro hemodynamic cast described bel "Cardiovascula Highly preferre include cardion endothelial and disorders that a such as diseases themselvas, such as disorders that a such as diseases themselvas, such a refreise, capillal and/or lymphati preferred are in	tion	ses	un/	tive	dis	lar s	ase,	per		', Va	ft v	ero	otic	s ne	int, o	yoc	nic	ver	low	r Di	d in	/asc	or a	syst	ffec	s me	jo;	h as	ries	ics)	dice
preferred in neoplastic d described by "Hyperportical provides by "Hyperportical provides by "Hyperportical provides by the cardiovas (e.g., heart failure anortic stenos cardiomyop regurgitation dysfunction and atherosa disease, dial intracardioa cardiomyop infarction, c hemodynam as described cardiorases (Fighly prefixed as discorders (e.g., heart failure anortical provides discorders discorde	lica	isea	low	fera	anc	scu	lise	, hy	sis,	athy	n, le	, ath	Slerc	etic	shu	m',	hro	iic c	l bel	ula	erre	diov	and,	έġ	at a	ete	ases	snc	illa	hat	e in
preferred neoplast describe "Hyperp "Hyperp Disorder the cardion the cardion cardion regurgit dysfunct and athe disease, intracard hypertro infarctic hemoty as descr "Cardio Highly grid include endothe disorder disorder disorder disorder and and referere	l in	ic d	d be	roli	(S,	lova	art c	lure	enos	yop	atio	tion	rose	dial	liac	phy	n, c	nan	ibed	vasc	ref	car	lial	s (e	s th	diat	dise	ves,	cap	ymp	d ar
pref desc "Hy, "Hy Disc (e.g. anti-  aorti card disc disc disc High hyp High hem as d "Ca High disc disc disc disc disc disc disc disc	erre	last	ribe	perp	rde	ard	, he	t fai	ic st	iom	rgit	inc	athe	ase,	car	ertro	rctic	ody	escr	rdio	hly 1	ude	othe	rder	rder	ı as	as	nsel	ries,	or l	erre
	ref	eof	jesc	'Hy	Disc	he (	(a)	near	aorti	card	regu	dysf	and	dise	intra	hype	infa	hem	as d	Ca	Hig	incl	ende	diso	diso	suck	wel]	ther	arte	and,	pref
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stimulate angiogenesis and/or	preferred are indications that	inhibit angiogenesis and/or	cardiovascularization.	Highly preferred indications	include antiangiogenic activity	to treat solid tumors,	leukemias, and Kaposi"s	sarcoma, and retinal disorders.	Highly preferred indications	include neoplasms and cancer,	such as, Kaposi"s sarcoma,	hemangioma (capillary and	cavernous), glomus tumors,	telangiectasia, bacillary	angiomatosis,	hemangioendothelioma,	angiosarcoma,	haemangiopericytoma,	lymphangioma,	lymphangiosarcoma. Highly	preferred indications also	include cancers such as,	prostate, breast, lung, colon,	pancreatic, esophageal,	stomach, brain, liver, and	urinary cancer. Preferred	indications include benign	dysproliferative disorders and	pre-neoplastic conditions, such
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as, for example, hyperplasia, metaplasia, and/or dysplasia. Highly preferred indications also include arterial disease, such as, atherosclerosis.	hypertension, coronary artery disease, inflammatory vasculitides, Reynaud"s disease and Reynaud"s phenomenom, aneurysms,	restenosis; venous and lymphatic disorders such as thrombophlebitis, lymphangitis, and lymphedema; and other vascular disorders such as	peripheral vascular disease, and cancer. Highly preferred indications also include trauma such as wounds, burns, and injured tissue (e.g., vascular injury such as, injury resulting from	atheroschlerotic lesions), implant fixation, scarring, ischemia reperfusion injury, rheumatoid arthritis, cerebrovascular disease, renal diseases such as acute renal failure, and osteoporosis.

Additional highly preferred	indications include stroke,	graft rejection, diabetic or	other retinopathies, thrombotic	and coagulative disorders,	vascularitis, lymph	angiogenesis, sexual disorders,	age-related macular	degeneration, and treatment	/prevention of endometriosis	and related conditions.	Additional highly preferred	indications include fibromas,	heart disease, cardiac arrest,	heart valve disease, and	vascular disease.	Preferred indications include	blood disorders (e.g., as	described below under	"Immune Activity", "Blood-	Related Disorders", and/or	"Cardiovascular Disorders").	Preferred indications include	autoimmune diseases (e.g.,	rheumatoid arthritis, systemic	lupus erythematosis, multiple	sclerosis and/or as described	below) and	immunodeficiencies (e.g., as	described below). Additional	preferred indications include
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ers (such ss, e.g., disease , and pain	I vention  I survival  T preferred  I vention  I survival.  Survival.  Ant of the  method  cyte  cyte  cyte  method  cyte  method  cyte  method  cyte  fremative  oodiment  des a  g  on. A  nt of the  method  cyte  method  cyte  des a  g  g  on. A  nt of the  method  weyte  method  cyte  method  cyte  method  g  g  g  g  nt of the  method  weyte  leternative  oodiment
inflammation and inflammatory disorders (such as acute and chronic inflammatory diseases, e.g., inflammatory bowel disease and Crohn's disease), and pain management.	A highly preferred embodiment of the invention includes a method for increasing adipocyte survival An alternative highly preferred embodiment of the invention includes a method for decreasing adipocyte survival. A preferred embodiment of the invention includes a method for stimulating adipocyte proliferation. An alternative highly preferred embodiment of the invention includes a method for inhibiting adipocyte proliferation. A preferred embodiment of the invention includes a method for stimulating adipocyte differentiation. An alternative highly preferred embodiment of the invention includes a method for stimulating adipocyte differentiation. An alternative highly preferred embodiment of the invention includes a method for inhibiting adipocyte differentiation.
	Kinase assay. Kinase assays, for example an GSK-3 assays, for PI3 kinase signal transduction that regulate glucose metabolism and cell survival are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote or inhibit glucose metabolism and cell survival. Exemplary assays for PI3 kinase activity that may be used or routinely modified to test PI3 kinase-induced activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Forrer et al., Biol Chem 379(8-9):1101-1110
	Activation of Kin Adipocyte P13 for Kinase Signalling for Pathway glu glu sur art rou the the the the ant ant ant ant ant ant pro me Ex, kin use tess of j inv and children in the the the Kin kin was and children in the the the Kin kin was and children in the the disk children in the the disk children in the the children in the the children in the c
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diabetes (e.g., diabetic	retinopathy, diabetic	nephropathy, kidney disease	(e.g., renal failure,	nephropathy and/or other	diseases and disorders as	described in the "Renal	Disorders" section below),	diabetic neuropathy, nerve	disease and nerve damage (e.g.,	due to diabetic neuropathy),	blood vessel blockage, heart	disease, stroke, impotence	(e.g., due to diabetic	neuropathy or blood vessel	blockage), seizures, mental	confusion, drowsiness,	nonketotic hyperglycemic-	hyperosmolar coma,	cardiovascular disease (e.g.,	heart disease, atherosclerosis,	microvascular disease,	hypertension, stroke, and other	diseases and disorders as	described in the	"Cardiovascular Disorders"	section below), dyslipidemia,	endocrine disorders (as	described in the "Endocrine	Disorders" section below),	neuropathy, vision impairment
diabet	retino	nephr	(e.g.,	nephr	diseas	descri	Disor	diaber	diseas	due to	boold	diseas	(e.g.,	neuro	block	confu	nonke	hyper	cardie	heart	micre	hypei	disea	descr	"Carc	sectic	endo	descr	Disor	nemu
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(e.g., diabetic retinopathy and blindness), ulcers and impaired wound healing, infection (e.g., infectious diseases and disorders as described in the	"Infectious Diseases" section below, especially of the urinary tract and skin), carpal tunnel syndrome and Dupuytren's contracture).  An additional highly preferred	complication is obesity and/or complications associated with obesity. Additional highly preferred indications include weight loss or alternatively, weight gain. Additional highly preferred indications are complications associated with insulin resistance.	Additional fights preferred indications are disorders of the musculoskeletal systems including myopathies, muscular dystrophy, and/or as described herein.  Additional highly preferred indications include, hypertension, coronary artery disease, dyslipidemia, gallstones, osteoarthritis,

		,			degenerative arthritis, eating
					and kidney diseases or
					disorders. Highly preferred
					indications include neoplasms
					and cancer, such as, lipoma,
_		_			liposarcoma, lymphoma,
					leukemia and breast, colon,
					and kidney cancer. Additional
					highly preferred indications
					include melanoma, prostate,
					lung, pancreatic, esophageal,
					stomach, brain, liver, and
		•			urinary cancer. Other preferred
					indications include benign
					dysproliferative disorders and
				•	pre-neoplastic conditions, such
					as, for example, hyperplasia,
					metaplasia, and/or dysplasia.
	HDPWU34	6201	Activation of	Assays for the activation of	Highly preferred indications
			transcription	transcription through the	include asthma, allergy,
			through GAS	Gamma Interferon Activation	hypersensitivity reactions,
			response element in	Site (GAS) response element	inflammation, and
			immune cells (such	are well-known in the art and	inflammatory disorders.
			as eosinophils).	may be used or routinely	Additional highly preferred
				modified to assess the ability	indications include immune
				of polypeptides of the	and hematopoietic disorders
				invention (including antibodies	(e.g., as described below under
				and agonists or antagonists of	"Immune Activity", and
				the invention) to modulate	"Blood-Related Disorders"),
_				gene expression (commonly	autoimmune diseases (e.g.,

rheumatoid arthritis, systemic lupus erythematosis, Crohn"s disease, multiple sclerosis	and/or as described below), immunodeficiencies (e.g., as	described below), boosting an eosinophil-mediated immune	response and, alternatively,	suppressing an eosinophil-	mediated minimus response.					_															
via STAT transcription factors) involved in a wide variety of cell functions. Exemplary	assays for transcription through the GAS response	element that may be used or routinely modified to test	GAS-response element activity	of polypeptides of the	and agonists or antagonists of	the invention) include assays	disclosed in Berger et al., Gene	66:1-10 (1998); Cullen and	Malm, Methods in Enzymol	216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA	85:6342-6346 (1988);	Matikainen et al., Blood	93(6):1980-1991 (1999); and	Henttinen et al., J Immunol	155(10):4582-4587 (1995); the	contents of each of which are	herein incorporated by	reference in its entirety.	Moreover, exemplary assays	that may be used or routinely	modified to assess the ability	of polypeptides of the	invention (including antibodies	and agonists or antagonists of
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the invention) to activate or inhibit activation of immune cells include assays disclosed and/or cited in: Mayumi M., "EoL-1, a human eosinophilic cell line" Leuk Lymphoma; Jun;7(3):243-50 (1992); Bhattacharya S, "Granulocyte macrophage colonystimulating factor and interleukin-5 activate STAT5 and induce CISI mRNA in human peripheral blood eosinophils" Am J Respir Cell Mol Biol, Mar;24(3):312-6 (2001); and, Du J, et al., "Engagement of the CrkL adapter in interleukin-5 signaling in eosinophils" J Biol Chem; Oct 20;275(42):33167-75 (2000); the contents of each of which are herein incorporated by reference in its entirety. Exemplary cells that may be used according to these assays include eosinophils. Eosinophils are a type of immune cell important in the late stage of allergic reactions; they are recruited to tissues and mastivactors.																															!
	the invention) to activate or	inhibit activation of immune	cells include assays disclosed	and/or cited in: Mayumi M.,	"EoL-1, a human eosinophilic	cell line" Leuk Lymphoma;	Jun;7(3):243-50 (1992);	Bhattacharya S, "Granulocyte	macrophage colony-	stimulating factor and	interleukin-5 activate STAT5	and induce CIS1 mRNA in	human peripheral blood	eosinophils" Am J Respir Cell	Mol Biol; Mar;24(3):312-6	(2001); and, Du J, et al.,	"Engagement of the CrkL	adapter in interleukin-5	signaling in eosinophils" J Biol	Chem; Oct 20;275(42):33167-	75 (2000); the contents of each	of which are herein	incorporated by reference in its	entirety. Exemplary cells that	may be used according to these	assays include eosinophils.	Eosinophils are a type of	immune cell important in the	late stage of allergic reactions;	they are recruited to tissues	and mediate the inflammtory
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response of late stage allergic reaction. Increases in GAS mediated transcription in eosinophils is typically a result of STAT activation, normally a direct consequence of interleukin or other cytokine receptor stimulation (e.g. IL3, IL5 or GMCSF).	Assays for the regulation (i.e. increases or decreases) of viability and proliferation of cells in vitro are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate viability and proliferation of pre-adipose cells and cell lines. For example, the CellTiter-Gloô Luminescent Cell Viability Assay (Promega Corp., Madison, WI, USA) can be used to measure the number of viable cells in culture based on quantitation of the ATP present which signals the present which signals the
	Proliferation of preadipose cells (such as 3T3-L1 cells)
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	HDPWU34
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active cells. 3T3-L1 is a mouse preadipocyte cell line. It is a continuous substrain of 3T3 fibroblast cells developed through clonal isolation. Cells were differentiated to an adipose-like state before being used in the screen. See Green H and Meuth M., Cell 3: 127-133 (1974), which is herein incorporated by reference in its entirety.	Assays for activation of transcription are well-known in the art and may be used and routinely modified to assess ability of polypeptides of the invention to inhibit or activate transcription. An example of such an assay follows: Cells were pretreated with SID supernatants or controls for 15-18 hours. SEAP activity was measured after 48 hours.  LS174T is an epithelial colon adenocarcinoma cell line. Its tumourigenicity in nude mice make cell line LS174T a model for studies on the mechanism of synthesis and secretion of synthesis and secretion of specific tumoral markers in
acti mo is a 3T? thry wer adi use H a 133	Activation of transcription that the rou abi involved transcription transcription the rou abi involved transcription transcripti
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НБОНБ03	1080	Production of IL-10 and activation of T-	colon cancer. See, Patan et al., Circ Res, 89(8):732-39 (2001), the contents of which are herein incorporated by reference in its entirety.  Assays for production of IL-10 and activation of T-cells are	Highly preferred indications include allergy and asthma.
		cells.	well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to stimulate or inhibit production of IL-10	Additional highly preferred indications include immune and hematopoietic disorders (e.g., as described below under "Immune Activity", and "Blood-Related Disorders"), autoimmune diseases (e.g., rheumatoid arthritis, systemic
			and/or activation of T-cells. Exemplary assays that may be used or routinely modified to assess the ability of polypeptides and antibodies of the invention (including agonists or antagonists of the invention) to modulate IL-10	lupus erythematosis, Crohn"s disease, multiple sclerosis and/or as described below), immunodeficiencies (e.g., as described below), boosting a T cell-mediated immune response, and suppressing a T cell-mediated immune
			production and on 1 cent proliferation include, for example, assays such as disclosed and/or cited in: Robinson, DS, et al., "Th-2 cytokines in allergic disease" Br Med Bull; 56 (4): 956-968 (2000), and Cohn, et al., "T-	

	Highly preferred indications include diabetes, myopathy, muscle cell atrophy, cancers of muscle (such as, rhabdomyoma, and
helper type 2 cell-directed therapy for asthma" Pharmacology & Therapeutics; 88: 187-196 (2000); the contents of each of which are herein incorporated by reference in their entirety. Exemplary cells that may be used according to these assays include Th2 cells. IL10 secreted from Th2 cells may be measured as a marker of Th2 cell activation. Th2 cells are a class of T cells that secrete IL4, IL10, IL13, IL5 and IL6. Factors that induce differentiation and activation of Th2 cells play a major role in the initiation and pathogenesis of allergy and asthma. Primary T helper 2 cells are generated via in vitro culture under Th2 polarizing conditions using peripheral blood lymphocytes isolated from cord blood.	Assays for muscle cell proliferation are well known in the art and may be used or routinely modified to assess the ability of polypeptides of
	Myoblast cell proliferation
	1081
	HDTBD53
	133

	the invention (including	rhabdosarcoma),
	antibodies and agonists or	cardiovascular disorders (such
	antagonists of the invention) to	as congestive heart failure,
	stimulate or inhibit myoblast	cachexia, myxomas, fibromas,
	cell proliferation. Exemplary	congenital cardiovascular
	assays for myoblast cell	abnormalities, heart disease,
	proliferation that may be used	cardiac arrest, heart valve
	or routinely modified to test	disease, vascular disease, and
	activity of polypeptides and	also as described below under
	antibodies of the invention	"Cardiovascular Disorders"),
	(including agonists or	stimulating myoblast
	antagonists of the invention)	proliferation, and inhibiting
	include, for example, assays	myoblast proliferation.
	disclosed in: Soeta, C., et al.	
	"Possible role for the c-ski	
 	gene in the proliferation of	
	myogenic cells in regenerating	
	skeletal muscles of rats" Dev	
	Growth Differ Apr;43(2):155-	
 	64 (2001); Ewton DZ, et al.,	
 	"IGF binding proteins-4, -5	
	and -6 may play specialized	
	roles during L6 myoblast	
	proliferation and	
	differentiation" J Endocrinol	
	Mar;144(3):539-53 (1995);	
	and, Pampusch MS, et	
	al.,"Effect of transforming	
	growth factor beta on	
	proliferation of L6 and	
	embryonic porcine myogenic	

				cells." J Cell Physiol Jun; 143(3):524-8 (1990); the contents of each of which are herein incorporated by reference in their entirety. Exemplary myoblast cells that may be used according to these assays include the rat myoblast L6 cell line. Rat myoblast L6 cells are an adherent rat myoblast cell line, isolated from primary cultures of rat thigh muscle, that fuse to form multinucleated myotubes and striated fibers after culture in	
134	HDTBP04	1082	Production of IL-6	IL-6 FMAT. IL-6 is produced by T cells and has strong effects on B cells. IL-6 participates in IL-4 induced IgE production and increases IgA production (IgA plays a role in mucosal immunity). IL-6 induces cytotoxic T cells. Deregulated expression of IL-6 has been linked to autoimmune disease, plasmacytomas, myelomas, and chronic hyperproliferative diseases. Assays for immunomodulatory and differentiation factor	A highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing) IL-6 production. An alternative highly preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) IL-6 production. A highly preferred indication is the stimulation or enhancement of mucosal immunity. Highly preferred indications include blood disorders (e.g., as described below under

d by a large "Immune Activity", "Blood- there the Related Disorders", and/or		kines, growth and infection (e.g., as				of autoimmune diseases (e.g.,	he invention   rheumatoid arthritis, systemic	dies and lupus erythematosis, multiple	onists of the sclerosis and/or as described		ion and immunodeficiencies (e.g., as		and function.   preferred indications also	s that test for include boosting a B cell-			IS IL-6, and B cell-mediated immune	nd response. Highly preferred	[ cell   indications include	functional inflammation and	assays that inflammatory		preferred indications include		ctivity of preferred indications include	he invention   neoplastic diseases (e.g.,	odies and myeloma, plasmacytoma,		
proteins produced by a large variety of cells where the	expression level is strongly	regulated by cytokines, growth	factors, and hormones are well	known in the art and may be	used or routinely modified to	assess the ability of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) to mediate	immunomodulation and	differentiation and modulate T	cell proliferation and function.	Exemplary assays that test for	immunomodulatory proteins	evaluate the production of	cytokines, such as IL-6, and	the stimulation and	upregulation of T cell	proliferation and functional	activities. Such assays that	may be used or routinely	modified to test	immunomodulatory and	diffferentiation activity of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include assays

neutrophilia, psoriasis, suppression of immune
--

					diabetes mellitus, endocarditis, meningitis, and Lyme Disease. An additonal preferred indication is infection (e.g., an infectious disease as described below under "Infectious
134	HDTBP04	1082	Production of MCP-1	MCP-1 FMAT. Assays for immunomodulatory proteins that are produced by a large variety of cells and act to induce chemotaxis and activation of monocytes and T cells are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mediate immunomodulation, induce chemotaxis, and modulate immune cell activation.  Exemplary assays that test for immunomodulatory proteins evaluate the production of cell surface markers, such as	A highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing) MCP-1 production. An alternative highly preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) MCP-1 production. A highly preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease"). Additional highly preferred indications include inflammation and inflammatory disorders. Preferred indications include blood disorders (e.g., as described below under
				protein (MCP), and the activation of monocytes and T cells. Such assays that may be	"Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders").

			used or routinely modified to	Highly preferred indications
			test immunomodulatory and	include autoimmune diseases
			differentiation activity of	(e.g., rheumatoid arthritis,
			polypeptides of the invention	systemic lupus erythematosis,
			(including antibodies and	multiple sclerosis and/or as
			agonists or antagonists of the	described below) and
			invention) include assays	immunodeficiencies (e.g., as
			disclosed in Miraglia et al., J	described below). Preferred
			Biomolecular Screening 4:193-	indications also include
			204(1999); Rowland et al.,	anemia, pancytopenia,
			"Lymphocytes: a practical	leukopenia, thrombocytopenia,
			approach" Chapter 6:138-160	Hodgkin's disease, acute
			(2000); Satthaporn and	lymphocytic anemia (ALL),
			Eremin, J R Coll Surg Ednb	plasmacytomas, multiple
			45(1):9-19 (2001); and	myeloma, Burkitt's lymphoma,
	•		Verhasselt et al., J Immunol	arthritis, AIDS, granulomatous
			158:2919-2925 (1997), the	disease, inflammatory bowel
			contents of each of which are	disease, sepsis, neutropenia,
-			herein incorporated by	neutrophilia, psoriasis,
			reference in its entirety.	suppression of immune
			Human dendritic cells that may	reactions to transplanted
	-		be used according to these	organs and tissues,
		-	assays may be isolated using	hemophilia, hypercoagulation,
	***		techniques disclosed herein or	diabetes mellitus, endocarditis,
			otherwise known in the art.	meningitis (bacterial and
			Human dendritic cells are	viral), Lyme Disease, asthma,
			antigen presenting cells in	and allergy Preferred
	-		suspension culture, which,	indications also include
			when activated by antigen	neoplastic diseases (e.g.,
			and/or cytokines, initiate and	leukemia, lymphoma, and/or as
	:		upregulate T cell proliferation	described below under

	are invention include using polypeptides of the invention odified (or antibodies, agonists, or antagonists thereof) in detection, diagnosis, of the Inflammation, Vascular CAM-1 Disease, Athereosclerosis, v assays Restenosis, and Stroke et al, 81  84  128  139  143  151  153  153  154  155  156  157  157  156  157  157  157
and functional activities.	Assays for measuring expression of ICAM-1 are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate ICAM-1 expression. Exemplary assays that may be used or routinely modified to measure ICAM-1 expression include assays disclosed in: Takacs P, et al, FASEB J, 15(2):279-281 (2001); and, Miyamoto K, et al., Am J Pathol, 156(5):1733-
	Production of ICAM-1
	1082
	HDTBP04
	134

	A highly preferred embodiment of the invention includes a method for stimulating endothelial cell growth. An alternative highly preferred embodiment of the invention includes a method for inhibiting endothelial cell growth. A highly preferred embodiment of the invention includes a method for stimulating endothelial cell proliferation. An alternative highly preferred embodiment of the invention includes a method for inhibiting endothelial cell proliferation. A highly preferred embodiment of the invention includes a method for inhibiting endothelial cell proliferation.
1739 (2000), the contents of each of which is herein incorporated by reference in its entirety. Cells that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary cells that may be used according to these assays include microvascular endothelial cells (MVEC).	Caspase Apoptosis. Assays for caspase apoptosis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote caspase protease-mediated apoptosis. Induction of apoptosis in endothelial cells supporting the vasculature of tumors is associated with tumor regression due to loss of tumor blood supply. Exemplary assays for caspase apoptosis that may be used or routinely modified to test capase
	Apoptosis
	1083
	HDTDQ23
	135

	apoptosis activity of	includes a method for
	polypeptides of the invention	stimulating apoptosis of
	(including antibodies and	endothelial cells. An
	agonists or antagonists of the	alternative highly preferred
	invention) include the assays	embodiment of the invention
	disclosed in Lee et al., FEBS	includes a method for
	Lett 485(2-3): 122-126 (2000);	inhibiting (e.g., decreasing)
~-	Nor et al., J Vasc Res 37(3):	apoptosis of endothelial cells.
	209-218 (2000); and Karsan	A highly preferred
	and Harlan, J Atheroscler	embodiment of the invention
	Thromb 3(2): 75-80 (1996);	includes a method for
	the contents of each of which	stimulating angiogenisis. An
	are herein incorporated by	alternative highly preferred
	reference in its entirety.	embodiment of the invention
	Endothelial cells that may be	includes a method for
	used according to these assays	inhibiting angiogenesis. A
	are publicly available (e.g.,	highly preferred embodiment
	through commercial sources).	of the invention includes a
	Exemplary endothelial cells	method for reducing cardiac
	that may be used according to	hypertrophy. An alternative
	these assays include bovine	highly preferred embodiment
	aortic endothelial cells	of the invention includes a
	(bAEC), which are an example	method for inducing cardiac
	of endothelial cells which line	hypertrophy. Highly
	blood vessels and are involved	preferred indications include
	in functions that include, but	neoplastic diseases (e.g., as
	are not limited to,	described below under
	angiogenesis, vascular	"Hyperproliferative
	permeability, vascular tone,	Disorders"), and disorders of
	and immune cell extravasation.	the cardiovascular system
		(e.g., heart disease, congestive

heart failure, hypertension, aortic stenosis, cardiomyopathy, valvular	regurgitation, left ventricular dysfunction, atherosclerosis and atherosclerotic vascular	disease, diabetic nephropainy, intracardiac shunt, cardiac hypertrophy, myocardial infarction, chronic	hemodynamic overload, and/or as described below under "Cardiovascular Disorders").	Highly preferred indications include cardiovascular, endothelial and/or angiogenic	disorders (e.g., systemic disorders that affect vessels such as diabetes mellitus, as well as diseases of the vessels	themselves, such as of the arteries, capillaries, veins and/or lymphatics). Highly preferred are indications that	stimulate angiogenesis and/or cardiovascularization. Highly preferred are indications that inhibit angiogenesis and/or	cardiovascularization. Highly preferred indications include antiangiogenic activity

to treat solid tumors,	leukemias, and Kaposi"s	sarcoma, and retinal disorders.	Highly preferred indications	include neoplasms and cancer,	such as, Kaposi"s sarcoma,	hemangioma (capillary and	cavernous), glomus tumors,	telangiectasia, bacillary	angiomatosis,	hemangioendothelioma,	angiosarcoma,	haemangiopericytoma,	lymphangioma,	lymphangiosarcoma. Highly	preferred indications also	include cancers such as,	prostate, breast, lung, colon,	pancreatic, esophageal,	stomach, brain, liver, and	urinary cancer. Preferred	indications include benign	dysproliferative disorders and	pre-neoplastic conditions, such	as, for example, hyperplasia,	metaplasia, and/or dysplasia.	Highly preferred indications	also include arterial disease,	such as, atherosclerosis,	hypertension, coronary artery	disease, inflammatory
														-																

vasculitides, Reynaud"s disease and Reynaud"s	phenomenom, aneurysms,	restenosis; venous and	lymphatic disorders such as	thrombophlebitis,	lymphangitis, and	lymphedema; and other	vascular disorders such as	peripheral vascular disease,	 preferred indications also	include trauma such as	wounds, burns, and injured	tissue (e.g., vascular injury	such as, injury resulting from	balloon angioplasty, and	atheroschlerotic lesions),	implant fixation, scarring,	ischemia reperfusion injury,	rheumatoid arthritis,	cerebrovascular disease, renal	diseases such as acute renal	failure, and osteoporosis.	Additional highly preferred	indications include stroke,	graft rejection, diabetic or	other retinopathies, thrombotic	and coagulative disorders,	vascularitis, lymph	angiogenesis, sexual disorders,
								-											****									
																		#- <b>-</b>						an an				

	HDTD023	1083	Stimulation of	Assays for measuring calcium	A highly preferred
175	2		Coloium Flux in	flux are well-known in the art	indication is diabetes mellitus.
133				and more to mood on continoty	An additional highly preferred
			pancreatic beta	and may be used or routinely	An additional inginy prefered
			cells.	modified to assess the ability	indication is a complication
				of polypeptides of the	associated with diabetes (e.g.,
				invention (including antibodies	diabetic retinopathy, diabetic
				and agonists or antagonists of	nephropathy, kidney disease
				the invention) to mobilize	(e.g., renal failure,
				calcium. For example, the	nephropathy and/or other
				FLPR assay may be used to	diseases and disorders as
				measure influx of calcium.	described in the "Renal
				Cells normally have very low	Disorders" section below),
				concentrations of cytosolic	diabetic neuropathy, nerve
				calcium compared to much	disease and nerve damage
				higher extracellular calcium.	(e.g., due to diabetic
				Extracellular factors can cause	neuropathy), blood vessel
				an influx of calcium, leading to	blockage, heart disease, stroke,
				activation of calcium	impotence (e.g., due to diabetic
				responsive signaling pathways	neuropathy or blood vessel
				and alterations in cell	blockage), seizures, mental
				functions. Exemplary assays	confusion, drowsiness,
				that may be used or routinely	nonketotic hyperglycemic-
				modified to measure calcium	hyperosmolar coma,
				flux by polypeptides of the	cardiovascular disease (e.g.,
				invention (including antibodies	heart disease, atherosclerosis,
				and agonists or antagonists of	microvascular disease,
			-	the invention) include assays	hypertension, stroke, and other
				disclosed in: Satin LS, et al.,	diseases and disorders as
				Endocrinology, 136(10):4589-	described in the
				601 (1995); Mogami H, et al.,	"Cardiovascular Disorders"
				Endocrinology, 136(7):2960-6	section below), dyslipidemia,

		(1995): Richardson SB. et al	endocrine disorders (as
		Biochem J, 288 (Pt 3):847-51	described in the "Endocrine
	-	(1992); and, Meats, JE, et al.,	Disorders" section below),
		Cell Calcium 1989 Nov-	neuropathy, vision impairment
		Dec;10(8):535-41 (1989), the	(e.g., diabetic retinopathy and
		contents of each of which is	blindness), ulcers and impaired
	***************************************	herein incorporated by	wound healing, and infection
		reference in its entirety.	(e.g., infectious diseases and
		Pancreatic cells that may be	disorders as described in the
		used according to these assays	"Infectious Diseases" section
		are publicly available (e.g.,	below, especially of the
		through the ATCC) and/or	urinary tract and skin), carpal
		may be routinely generated.	tunnel syndrome and
		Exemplary pancreatic cells that	Dupuytren's contracture).
		may be used according to these	An additional highly preferred
		assays include HITT15 Cells.	indication is obesity and/or
-		HITT15 are an adherent	complications associated with
		epithelial cell line established	obesity. Additional highly
		from Syrian hamster islet cells	preferred indications include
		transformed with SV40. These	weight loss or alternatively,
		cells express glucagon,	weight gain. Aditional
Print to the		somatostatin, and	highly preferred indications are
		glucocorticoid receptors. The	complications associated with
		cells secrete insulin, which is	insulin resistance.
		stimulated by glucose and	
		glucagon and suppressed by	
		somatostatin or	
		glucocorticoids. ATTC# CRL-	
		1777 Refs: Lord and	
		Ashcroft. Biochem. J. 219:	
		547-551; Santerre et al. Proc.	

	A highly preferred	embodiment of the invention	includes a method for	stimulating the production of	IFNg. An alternative highly	preferred embodiment of the	invention includes a method	for inhibiting the production of	IFNg. Highly preferred	indications include blood	disorders (e.g., as described	below under "Immune	Activity", "Blood-Related	Disorders",	"Hyperproliferative Disorders"	(e.g. cancer/tumorigenesis)	and/or "Cardiovascular	Disorders"), and infection	(e.g., viral infections,	tuberculosis, infections	associated with chronic	granulomatosus disease and	malignant osteoporosis, and/or	as described below under	"Infectious Disease"). Highly	preferred indications include	autoimmune disease (e.g.,	rheumatoid arthritis, systemic	lupus erythematosis, multiple
Natl. Acad. Sci. USA 78: 4339-4343. 1981.	IFNgamma FMAT. IFNg	plays a central role in the	immune system and is	considered to be a	proinflammatory cytokine.	IFNg promotes TH1 and	inhibits TH2; promotes IgG2a	and inhibits IgE; induces	macrophage activation; and	increases MHC expression.	Assays for immunomodulatory	proteins produced by T cells	and NK cells that regulate a	variety of inflammatory	activities and inhibit TH2	helper cell functions are well	known in the art and may be	used or routinely modified to	assess the ability of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) to mediate	immunomodulation, regulate	inflammatory activities,	modulate TH2 helper cell	function, and/or mediate	humoral or cell-mediated	immunity. Exemplary assays
	Production of	IFNgamma using	Natural Killer cells															****						-					
	1084																												
	HDTEK44																												
		136																	·										

that test for	sclerosis and/or as described
immunomodulatory proteins	below), immunodeficiency
evaluate the production of	(e.g., as described below),
cytokines, such as Interferon	boosting a T cell-mediated
gamma (IFNg), and the	immune response, and
activation of T cells. Such	suppressing a T cell-mediated
assays that may be used or	immune response, boosting
routinely modified to test	antibody-dependent immune
immunomodulatory activity of	responses, suppressing
polypeptides of the invention	antibody-dependent immune
(including antibodies and	responses, boosting innate
agonists or antagonists of the	immunity and immune
invention) include the assays	responses, and suppressing
disclosed in Miraglia et al., J	innate immunity and immune
Biomolecular Screening 4:193-	responses. Additional highly
204 (1999); Rowland et al.,	preferred indications include
"Lymphocytes: a practical	inflammation and
approach" Chapter 6:138-160	inflammatory disorders.
(2000); Gonzalez et al., J Clin	Additional preferred
Lab Anal 8(5):225-233 (1995);	indications include idiopathic
Billiau et al., Ann NY Acad	pulmonary fibrosis. Highly
Sci 856:22-32 (1998); Boehm	preferred indications include
et al., Annu Rev Immunol	neoplastic diseases (e.g.,
15:749-795 (1997), and	leukemia, lymphoma,
Rheumatology (Oxford)	melanoma, and/or as described
38(3):214-20 (1999), the	below under
contents of each of which are	"Hyperproliferative
herein incorporated by	Disorders"). Highly preferred
reference in its entirety.	indications include neoplasms
Natural Killer (NK) cells that	and cancers, such as, for
may be used according to these	example, leukemia, lymphoma,

				assays are miblicly available	melanoma and prostate.
				(e a through the ATCC) or	breast lung colon pancreatic.
				may be isolated using	esophageal, stomach, brain,
,				techniques disclosed herein or	liver and urinary cancer. Other
				otherwise known in the art.	preferred indications include
				Natural killer (NK) cells are	benign dysproliferative
				large granular lymphocytes	disorders and pre-neoplastic
				that have cytotoxic activity but	conditions, such as, for
				do bind antigen. NK cells	example, hyperplasia,
				show antibody-independent	metaplasia, and/or dysplasia.
				killing of tumor cells and also	Preferred indications include
				recognize antibody bound on	anemia, pancytopenia,
				target cells, via NK Fc	leukopenia, thrombocytopenia,
				receptors, leading to cell-	Hodgkin's disease, acute
				mediated cytotoxicity.	lymphocytic anemia (ALL),
					plasmacytomas, multiple
					myeloma, Burkitt's lymphoma,
					arthritis, AIDS, granulomatous
					disease, inflammatory bowel
					disease, sepsis, neutropenia,
					neutrophilia, psoriasis,
					suppression of immune
			-1-		reactions to transplanted
					organs and tissues,
					hemophilia, hypercoagulation,
					diabetes mellitus, endocarditis,
			***		meningitis, Lyme Disease,
					asthma and allergy.
137	HDTEN81	1085	CD152 in Human T		
	HDTFE17	1086	Activation of	Assays for the activation of	Highly preferred indications

include blood disorders (e.g., as described below under "Immune Activity", "Blood-	Related Disorders", and/or "Cardiovascular Disorders"). Highly preferred indications include autoimmine diseases	(e.g., rheumatoid arthritis, systemic lupus erythematosis,	multiple sclerosis and/or as described below),	immunodeficiencies (e.g., as described below), boosting a T	cell-mediated immune	response, and suppressing a 1 cell-mediated immune	response. Additional highly	preferred indications include inflammation and	inflammatory disorders. An	additional highly preferred	infections disease as described	below under "Infectious	Disease"). Preferred	indications include neoplastic	diseases (e.g., leukemia,	lymphoma, and/or as described	below under	"Hyperproliferative	Disorders"). Preferred
transcription through the Nuclear Factor of Activated T cells (NFAT) response element	are well-known in the art and may be used or routinely modified to assess the ability of not wantides of the	invention (including antibodies and agonists or antagonists of	the invention) to regulate NFAT transcription factors and	modulate expression of genes involved in	immunomodulatory functions.	Exemplary assays for transcription through the	NFAT response element that	may be used or routinely modified to test NFAT-	response element activity of	polypeptides of the invention	(including antibodies and agonists of the	invention) include assays	disclosed in Berger et al., Gene	66:1-10 (1998); Cullen and	Malm, Methods in Enzymol	216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA	85:6342-6346 (1988);	Aramburu et al., J Exp Med
transcription through NFAT response element in	as natural killer cells).					. ,,_													
138																			

			182(3):801-810 (1995); De	indications include neoplasms
			Boer et al., Int J Biochem Cell	and cancers, such as, for
			Biol 31(10):1221-1236 (1999);	example, leukemia, lymphoma,
			Fraser et al., Eur J Immunol	and prostate, breast, lung,
			29(3):838-844 (1999); and	colon, pancreatic, esophageal,
			Yeseen et al., J Biol Chem	stomach, brain, liver and
			268(19):14285-14293 (1993),	urinary cancer. Other preferred
			the contents of each of which	indications include benign
			are herein incorporated by	dysproliferative disorders and
			reference in its entirety. NK	pre-neoplastic conditions, such
	27884		cells that may be used	as, for example, hyperplasia,
			according to these assays are	metaplasia, and/or dysplasia.
			publicly available (e.g.,	Preferred indications also
	V-2		through the ATCC).	include anemia, pancytopenia,
			Exemplary human NK cells	leukopenia, thrombocytopenia,
			that may be used according to	Hodgkin's disease, acute
			these assays include the NK-	lymphocytic anemia (ALL),
			YT cell line, which is a human	plasmacytomas, multiple
			natural killer cell line with	myeloma, Burkitt's lymphoma,
			cytolytic and cytotoxic	arthritis, AIDS, granulomatous
			activity.	disease, inflammatory bowel
				disease, sepsis, neutropenia,
				neutrophilia, psoriasis,
1				suppression of immune
				reactions to transplanted
				organs and tissues,
•				hemophilia, hypercoagulation,
				diabetes mellitus, endocarditis,
	*********			meningitis, Lyme Disease,
			100000000000000000000000000000000000000	asthma and allergy.
HDTGC73	1087	Production of	Assays for measuring	Preferred embodiments of the

139			ICAM-1	expression of ICAM-1 are	invention include using
				well-known in the art and may	polypeptides of the invention
				be used or routinely modified	(or antibodies, agonists, or
				to assess the ability of	antagonists thereof) in
				polypeptides of the invention	detection, diagnosis,
				including antibodies and	prevention, and/or treatment of
				agonists or antagonists of the	Inflammation, Vascular
				invention) to regulate ICAM-1	Disease, Athereosclerosis,
			)	expression. Exemplary assays	Restenosis, and Stroke
				that may be used or routinely	
				modified to measure ICAM-1	
				expression include assays	
				disclosed in: Takacs P, et al,	
				FASEB J, 15(2):279-281	·
				(2001); and, Miyamoto K, et	
				al., Am J Pathol, 156(5):1733-	
				1739 (2000), the contents of	
				each of which is herein	
				incorporated by reference in its	
				entirety. Cells that may be	
				used according to these assays	
				are publicly available (e.g.,	
				through the ATCC) and/or	
			,	may be routinely generated.	
				Exemplary cells that may be	
				used according to these assays	
				include microvascular	
				endothelial cells (MVEC).	
	HDTIT10	1088	Production of IL-6	IL-6 FMAT. IL-6 is produced	A highly preferred
140				by T cells and has strong	embodiment of the invention
	(v)4/2 ()		i morphism	effects on B cells. IL-6	includes a method for

stimulating (e.g., increasing) IL-6 production. An alternative highly preferred embodiment of the invention includes a method for inhibiting (e.g.,	reducing) IL-6 production. A highly preferred indication is the stimulation or enhancement	of mucosal immunity. Highly preferred indications include blood disorders (e.g., as	"Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"),	and infection (e.g., as described below under "Infectious Disease"). Highly preferred indications include autoimmune diseases (e.g.,	rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below) and	immunodeficiencies (e.g., as described below). Highly preferred indications also include boosting a B cellmediated immune response and alternatively suppressing a B cell-mediated immune
participates in IL-4 induced IgE production and increases IgA production (IgA plays a role in mucosal immunity). IL-6 induces evtotoxic T cells.	Deregulated expression of IL-6 has been linked to autoimmune disease, plasmacytomas,	hyperproliferative diseases. Assays for immunomodulatory	proteins produced by a large variety of cells where the expression level is strongly	regulated by cytokines, growth factors, and hormones are well known in the art and may be used or routinely modified to assess the ability of	polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mediate	immunomodulation and differentiation and modulate T cell proliferation and function. Exemplary assays that test for immunomodulatory proteins evaluate the production of cytokines, such as IL-6, and

				and/or cytokines, initiate and upregulate T cell proliferation and functional activities.	Hodgkin's disease, acute lymphocytic anemia (ALL), multiple myeloma. Burkitt's
					lymphoma, arthritis, AIDS, granulomatous disease,
					inflammatory bowel disease,
					sepsis, iredu openia, neutrophilia, psoriasis,
					suppression of immune
					reactions to transplanted
					organs and tissues,
					hemophilia, hypercoagulation,
					diabetes mellitus, endocarditis,
					meningitis, and Lyme Disease.
					An additonal preferred
					indication is infection (e.g., an
					infectious disease as described
					below under "Infectious
				1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1	Disease").
	HDTIT10	1088	SEAP in		
140			HepG2/Squale-		
			synthetase(stimulati on)		
	HDTMK50	1089	Activation of	Kinase assay. Kinase assays,	A highly preferred
141			Natural Killer Cell	for example an Elk-1 kinase	embodiment of the invention
			ERK Signaling	assay, for ERK signal	includes a method for
			Pathway.	transduction that regulate cell	stimulating natural killer cell
				proliferation or differentiation	proliferation. An alternative
				are well known in the art and	highly preferred embodiment
	-			may be used or routinely	of the invention includes a
				modified to assess the ability	method for inhibiting natural

n. A odiment ides a ng natural ion. An eferred	invention for iller cell Highly ns include (e.g., as	sorders low under orders", d disorders	low under and seribed ous lood scribed le scribed scribed scribed seribed seri
killer cell proliferation. A highly preferred embodiment of the invention includes a method for stimulating natural killer cell differentiation. An alternative highly preferred	embodiment of the invention includes a method for inhibiting natural killer cell differentiation. Highly preferred indications include neoplastic diseases (e.g., as	described below under "Hyperproliferative Disorders"), blood disorders (e.g., as described below under "Immune Activity", "Cardiovascular Disorders", and/or "Blood-Related Disorders"), immune disorders	(e.g., as described below under "Immune Activity") and infections (e.g., as described below under "Infectious Disease"). Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders").
of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote or inhibit cell proliferation, activation, and differentiation.	Exemplary assays for ERK kinase activity that may be used or routinely modified to test ERK kinase-induced activity of polypeptides of the invention (including antibodies	and agonists or antagonists of the invention) include the assays disclosed in Forrer et al., Biol Chem 379(8-9):1101- 1110 (1998); Kyriakis JM, Biochem Soc Symp 64:29-48 (1999); Chang and Karin, Nature 410(6824):37-40	Biophys Mol Biol 71(3-4):479-500 (1999); the contents of each of which are herein incorporated by reference in its entirety. Natural killer cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary natural killer cells that may be used
5.2 6 5.2 6			

a a	according to these assays include the human natural	Highly preferred indications include autoimmune diseases
X	killer cell lines (for example,	(e.g., rheumatoid arthritis,
	NK-Y I cells which have	systemic lupus erythematosis,
<u>г. ж</u>	cytolytic and cytoloxic activity) or primary NK cells.	multiple scierosis and/or as described below) and
		immunodeficiencies (e.g., as
		described below). Additional
		highly preferred indications
		include inflammation and
		inflammatory disorders.
		Highly preferred indications
		also include cancers such as,
		kidney, melanoma, prostate,
		breast, lung, colon, pancreatic,
		esophageal, stomach, brain,
		liver, urinary cancer,
		lymphoma and leukemias.
		Other preferred indications
		include benign dysproliferative
		disorders and pre-neoplastic
		conditions, such as, for
		example, hyperplasia,
		metaplasia, and/or dysplasia.
		Other highly preferred
		indications include,
		pancytopenia, leukopenia,
		leukemias, Hodgkin's disease,
		acute lymphocytic anemia
		(ALL), arthritis, asthma,
		AIDS, granulomatous disease,

says ins f f ron tr r tr t	ss so s	ns ss so	y of on he
function, and/or mediate humoral or cell-mediated immunity. Exemplary assays that test for immunomodulatory proteins evaluate the production of cytokines, such as Interferon gamma (IFNg), and the activation of T cells. Such assays that may be used or routinely modified to test immunomodulatory activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include the assays disclosed in Miraglia et al., J Biomolecular Screening 4:193-204 (1999); Rowland et al., "Lymphocytes: a practical approach" Chapter 6:138-160 (2000); Gonzalez et al., J Clin Lab Anal 8(5):225-233 (1995); Billiau et al., Ann NY Acad Sci 856:22-32 (1998); Boehm et al., Annu Rev Immunol 15:749-795 (1997), and	function, and/or mediate humoral or cell-mediated immunity. Exemplary assays that test for immunomodulatory proteins evaluate the production of cytokines, such as Interferon gamma (IFNg), and the activation of T cells. Such assays that may be used or routinely modified to test immunomodulatory activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include the assays disclosed in Miraglia et al., J Biomolecular Screening 4:193- 204 (1999); Rowland et al., "Lymphocytes: a practical approach" Chapter 6:138-160 (2000); Gonzalez et al., J Clin Lab Anal 8(5):225-233 (1995); Billiau et al., Ann NY Acad Sci 856:22-32 (1998); Boehm et al., Annu Rev Immunol 15:749-795 (1997), and	function, and/or mediate humoral or cell-mediated immunity. Exemplary assays that test for immunomodulatory proteins evaluate the production of cytokines, such as Interferon gamma (IFNg), and the activation of T cells. Such assays that may be used or routinely modified to test immunomodulatory activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include the assays disclosed in Miraglia et al., J Biomolecular Screening 4:193- 204 (1999); Rowland et al., "Lymphocytes: a practical approach" Chapter 6:138-160 (2000); Gonzalez et al., J Clin Lab Anal 8(5):225-233 (1995); Billiau et al., Ann NY Acad Sci 856:22-32 (1998); Boehm et al., Annu Rev Immunol 15:749-795 (1997), and	function, and/or mediate humoral or cell-mediated immunity. Exemplary assays that test for immunomodulatory proteins evaluate the production of cytokines, such as Interferon gamma (IFNg), and the activation of T cells. Such assays that may be used or routinely modified to test immunomodulatory activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include the assays disclosed in Miraglia et al., J Biomolecular Screening 4:193- 204 (1999); Rowland et al., "Lymphocytes: a practical approach" Chapter 6:138-160 (2000); Gonzalez et al., J Clin Lab Anal 8(5):225-233 (1995); Billiau et al., Ann NY Acad Sci 856:22-32 (1998); Boehm et al., Annu Rev Immunol
function, and/or mediate humoral or cell-mediate humoral or cell-mediate immunity. Exemplary a that test for immunomodulatory protevaluate the production cytokines, such as Interfigamma (IFNg), and the activation of T cells. Su assays that may be used routinely modified to test immunomodulatory actipolypeptides of the inversional polypeptides of th	function, and/or in humoral or cell-m immunity. Exemy that test for immunomodulato evaluate the producytokines, such as gamma (IFNg), ar activation of T cel assays that may be routinely modified immunomodulato polypeptides of the (including antibod agonists or antago invention) include disclosed in Mirag Biomolecular Scr 204 (1999); Rowl "Lymphocytes: a papproach" Chapte (2000); Gonzalez Lab Anal 8(5):225 Billiau et al., Ann Sci 856:22-32 (19 et al., Annu Rev I 15:749-795 (1997)	function, and/or in humoral or cell-m immunity. Exemy that test for immunomodulato evaluate the producytokines, such as gamma (IFNg), ar activation of T cel assays that may be routinely modified immunomodulato polypeptides of the (including antibod agonists or antago invention) included disclosed in Mirag Biomolecular Scre 204 (1999); Rowls "Lymphocytes: a paproach" Chapte (2000); Gonzalez Lab Anal 8(5):222 Billiau et al., Ann Sci 856:22-32 (1997); Sign 15:749-795 (1997); Ci 1997	function, and/or inmunity. Exempt that test for immunomodulator evaluate the production and that test for immunomodulator evaluate the production of the cytokines, such as gamma (IFNg), at activation of T celassays that may be routinely modified immunomodulator polypeptides of the (including antibod agonists or antago invention) included disclosed in Mirag Biomolecular Scra 204 (1999); Rowll "Lymphocytes: a papproach" Chapte (2000); Gonzalez Lab Anal 8(5):222 Billiau et al., Ann Sci 856:22-32 (1997); Royll 15:749-795 (1997); Royll 15:749-79

				herein incorporated by	disorders and pre-neoplastic
				reference in its entirety.	conditions, such as, for
				Human T cells that may be	example, hyperplasia,
				used according to these assays	metaplasia, and/or dysplasia.
				may be isolated using	Preferred indications include
				techniques disclosed herein or	anemia, pancytopenia,
				otherwise known in the art.	leukopenia, thrombocytopenia,
				Human T cells are primary	Hodgkin's disease, acute
				human lymphocytes that	lymphocytic anemia (ALL),
				mature in the thymus and	plasmacytomas, multiple
				express a T Cell receptor and	myeloma, Burkitt's lymphoma,
				CD3, CD4, or CD8. These	arthritis, AIDS, granulomatous
				cells mediate humoral or cell-	disease, inflammatory bowel
				mediated immunity and may	disease, sepsis, neutropenia,
				be preactivated to enhance	neutrophilia, psoriasis,
				responsiveness to	suppression of immune
				immunomodulatory factors.	reactions to transplanted
					organs and tissues,
					hemophilia, hypercoagulation,
					diabetes mellitus, endocarditis,
					meningitis, Lyme Disease,
					asthma and allergy.
	HE2EB74	1091	Activation of	Kinase assay. JNK and p38	A highly preferred
143			Endothelial Cell	kinase assays for signal	embodiment of the invention
			p38 or JNK	transduction that regulate cell	includes a method for
			Signaling Pathway.	proliferation, activation, or	stimulating endothelial cell
				apoptosis are well known in	growth. An alternative highly
				the art and may be used or	preferred embodiment of the
				routinely modified to assess	invention includes a method
				the ability of polypeptides of	for inhibiting endothelial cell
				the invention (including	growth. A highly preferred

	antibodies and agonists or	embodiment of the invention
	antagonists of the invention) to	includes a method for
	promote or inhibit cell	stimulating endothelial cell
	proliferation, activation, and	proliferation. An alternative
	apoptosis. Exemplary assays	highly preferred embodiment
	for JNK and p38 kinase	of the invention includes a
	activity that may be used or	method for inhibiting
	routinely modified to test JNK	endothelial cell proliferation.
	and p38 kinase-induced	A highly preferred
	activity of polypeptides of the	embodiment of the invention
	invention (including antibodies	includes a method for
•	and agonists or antagonists of	stimulating apoptosis of
	the invention) include the	endothelial cells. An
	assays disclosed in Forrer et	alternative highly preferred
	al., Biol Chem 379(8-9):1101-	embodiment of the invention
	1110 (1998); Gupta et al., Exp	includes a method for
-	Cell Res 247(2): 495-504	inhibiting (e.g., decreasing)
	(1999); Kyriakis JM, Biochem	apoptosis of endothelial cells.
-	Soc Symp 64:29-48 (1999);	A highly preferred
	Chang and Karin, Nature	embodiment of the invention
	410(6824):37-40 (2001); and	includes a method for
	Cobb MH, Prog Biophys Mol	stimulating (e.g., increasing)
	Biol 71(3-4):479-500 (1999);	endothelial cell activation. An
	the contents of each of which	alternative highly preferred
	are herein incorporated by	embodiment of the invention
	reference in its entirety.	includes a method for
	Endothelial cells that may be	inhibiting (e.g., decreasing) the
	used according to these assays	activation of and/or
	are publicly available (e.g.,	inactivating endothelial cells.
	through the ATCC).	A highly preferred
	Exemplary endothelial cells	embodiment of the invention

includes a method for	stimulating angiogenisis. An	alternative highly preferred	embodiment of the invention	includes a method for	inhibiting angiogenesis. A	highly preferred embodiment	of the invention includes a	method for reducing cardiac	hypertrophy. An alternative	highly preferred embodiment	of the invention includes a	method for inducing cardiac	hypertrophy. Highly	preferred indications include	neoplastic diseases (e.g., as	described below under	"Hyperproliferative	Disorders"), and disorders of	the cardiovascular system	(e.g., heart disease, congestive	heart failure, hypertension,	aortic stenosis,	cardiomyopathy, valvular	regurgitation, left ventricular	dysfunction, atherosclerosis	and atherosclerotic vascular	disease, diabetic nephropathy,	intracardiac shunt, cardiac	hypertrophy, myocardial infarction chronic
that may be used according to	these assays include human	umbilical vein endothelial cells	(HUVEC), which are	endothelial cells which line	venous blood vessels, and are	involved in functions that	include, but are not limited to,	angiogenesis, vascular	permeability, vascular tone,	and immune cell extravasation.																			
								-		***																			

hemangioendothelioma, angiosarcoma, haemangiopericytoma, lymphangioma, lymphangiosarcoma. Highly	preferred indications also include cancers such as, prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver, and	urinary cancer. Preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia,	Highly preferred indications also include arterial disease, such as, atherosclerosis, hypertension, coronary artery disease, inflammatory vasculitides, Reynaud"s disease and Reynaud"s	phenomenom, aneurysms, restenosis; venous and lymphatic disorders such as thrombophlebitis, lymphangitis, and lymphedema; and other vascular disorders such as peripheral vascular disease,

and cancer. Highly preferred indications also include trauma such as wounds, burns, and injured	tissue (e.g., vascular injury such as, injury resulting from balloon angioplasty, and atheroschlerotic lesions), implant fixation, scarring, ischemia reperfusion injury,	cerebrovascular disease, renal diseases such as acute renal failure, and osteoporosis.  Additional highly preferred indications include stroke, graft rejection, diabetic or other retinopathies, thrombotic and coagulative disorders, vascularitis, lymph	angiogenesis, sexual disorders, age-related macular degeneration, and treatment /prevention of endometriosis and related conditions.  Additional highly preferred indications include fibromas, heart disease, cardiac arrest, heart valve disease, and vascular disease.  Preferred indications include

				blood disorders (e.g., as
				described below under
				"Immune Activity", "Blood-
				Related Disorders", and/or
				"Cardiovascular Disorders").
				Preferred indications include
				autoimmune diseases (e.g.,
				rheumatoid arthritis, systemic
				lupus erythematosis, multiple
				sclerosis and/or as described
				below) and
				immunodeficiencies (e.g., as
				described below). Additional
				preferred indications include
<b>2.</b>				inflammation and
				inflammatory disorders (such
				as acute and chronic
				inflammatory diseases, e.g.,
				inflammatory bowel disease
				and Crohn's disease), and pain
			the promote property control of the second o	management.
HEZEN04	1092	Activation of JNK	Kinase assay. JNK kinase	Highly preferred indications
		Signaling Pathway	assays for signal transduction	include asthma, allergy,
		in immune cells	that regulate cell proliferation,	hypersensitivity reactions,
		(such as	activation, or apoptosis are	inflammation, and
		eosinophils).	well known in the art and may	inflammatory disorders.
			be used or routinely modified	Additional highly preferred
			to assess the ability of	indications include immune
			polypeptides of the invention	and hematopoietic disorders
	_		(including antibodies and	(e.g., as described below under
			agonists or antagonists of the	"Immune Activity", and

invention) to promote or inhibit cell proliferation, aud apoptosis.  Exemplary assays for JMK kinase-induced advantages (e.g., activation, and apoptosis. Exemplary assays for JMK kinase-induced advantage activity that may be disease, multiple soferosis used or routinely modified to immunodeficiencies (e.g., as activity of polypeptides of the immunodeficiencies (e.g., as activity of polypeptides of the immunodeficiencies (e.g., as activity of polypeptides of the described below). Highly invention (including antibodies preferred indications also and agonists or antagonists of include boosting or inhibiting the invention) include the assays described below. Highly invention (including antibodies preferred indications include a.l., Biot Chem 379(8-9):1101 — neoplastic diseases (e.g., 110 (1988); Gupta et al., Exp. Heternati, Jumphoma, and/or as Cell Res 547(2):495-504 (1999); Gubt Al., Prog Biophys Mol Rescribed below under 40(0824):3740 (2001); and Cosinophil. Resinophil mediated immune Cobb MH, Prog Biophys Mol response, and suppressing an are hereni incorporated by reference in its entirety. Exemplary cells that may be used according to these assays include eosinophilis. Ecsinophilis are important in the late stage of allergic reactions; they are recruited to
invention) to promote or inhibit cell proliferation, activation, and apoptosis.  Exemplate assays for JNK kinase activity that may be used or routinely modified to test JNK kinase-induced activity of polypeptides of the invention (including antibodies and agonists or antagonists or antagonists or the invention) include the assays disclosed in Forrer et al., Biol Chem 379(8-9):1101-1110 (1998); Gupta et al., Exp Cell Res 247(2): 495-504 (1999); Clang and Karin, Nature 410(6824):37-40 (2001); and Cobb MH, Prog Biophys Mol Biol 71(3-4):479-500 (1999); the contents of each of which are therein incorporated by reference in its entirety.  Exemplaty cells that may be used according to these assays include eosinophils.  Eosinophils are important in the late stage of allergic reactions; they are recruited to tissues and mediate the cissues and mediate the

inflammatory response of late stage allergic reaction.  Moreover, exemplary assays that may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to modulate signal transduction, cell proliferation, activation, or apoptosis in eosinophils include assays disclosed and/or cited in: Zhang JP, et al., "Role of caspases in dexamethasone-induced apoptosis and activation of c-Jun NH2-terminal kinase and p38 mitogen-activated protein kinase and p38 mitogen-activated protein (Distruption of fas receptor signaling by nitric oxide in eosinophils." "Distruption of fas receptor signaling by nitric oxide in eosinophils." Jexp Med; Feb 2;187(3):415-25 (1998); J Allergy Clin Immunol 1999 Sep;104(3 Pt 1):565-74; and, Sousa AR, et al., "In vivo																																
	inflammatory response of late	stage allergic reaction	stage allergic reaction.	Moreover, exemplary assays	that may be used or routinely	modified to assess the ability	of polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) to modulate	signal transduction, cell	proliferation, activation, or	apoptosis in eosinophils	include assays disclosed and/or	cited in: Zhang JP, et al., "Role	of caspases in dexamethasone-	induced apoptosis and	activation of c-Jun NH2-	terminal kinase and p38	mitogen-activated protein	kinase in human eosinophils"	Clin Exp Immunol;	Oct;122(1):20-7 (2000);	Hebestreit H, et al.,	"Disruption of fas receptor	signaling by nitric oxide in	eosinophils" J Exp Med; Feb	2;187(3):415-25 (1998); J	Allergy Clin Immunol 1999	Sep;104(3 Pt 1):565-74; and,	Sousa AR, et al., "In vivo	resistance to corticosteroids in
					<u> </u>																			and the State of								

	Preferred embodiments of the invention include using polypeptides of the invention (or antibodies, agonists, or antagonists thereof) in detection, diagnosis, prevention, and/or treatment of Vascular Disease, Atherosclerosis, Restenosis, Stroke, and Asthma.
bronchial asthma is associated with enhanced phosyphorylation of JUN N-terminal kinase and failure of prednisolone to inhibit JUN N-terminal kinase phosphorylation" J Allergy Clin Immunol; Sep;104(3 Pt 1):565-74 (1999); the contents of each of which are herein incorporated by reference in its entirety.	Assays for measuring expression of ICAM-1 are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate ICAM-1 expression. Exemplary assays that may be used or routinely modified to measure ICAM-1 expression include assays disclosed in: Rolfe BE, et al., Atherosclerosis, 149(1):99-110 (2000); Panettieri RA Jr, et al., J Immunol, 154(5):2358-2365 (1995); and, Grunstein MM, et al., Am J Physiol Lung Cell
	Production of ICAM-1
	1093
	HE2FV03
	1174

		Preferred indications include neoplastic diseases (e.g., as described below under "Hyperproliferative Disorders"), blood disorders (e.g., as described below under "Immune Activity", "Cardiovascular Disorders", and/or "Blood-Related Disorders"), and infection (e.g., an infectious disease as described below under "Infectious Disease"). Highly preferred indications include autoimmune diseases (e.g.
Mol Physiol, 278(6):L1154-L1163 (2000), the contents of each of which is herein incorporated by reference in its entirety. Cells that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary cells that may be used according to these assays include Aortic Smooth Muscle Cells (AOSMC); such as bovine AOSMC.		Kinase assay. JNK and p38 kinase assays for signal transduction that regulate cell proliferation, activation, or apoptosis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote or inhibit immune cell (e.g. T-cell) proliferation, activation, and apoptosis.
	SEAP in OE-33	Activation of T-Cell p38 or JNK Signaling Pathway.
	1093	1094
	HE2FV03	HE2NV57
	145	146

p38 kinase activity that may be	rheumatoid arthritis, systemic
 used or routinely modified to	lupus erythematosis, multiple
test JNK and p38 kinase-	sclerosis and/or as described
induced activity of	below) and
polypeptides of the invention	immunodeficiencies (e.g., as
(including antibodies and	described below). Additional
agonists or antagonists of the	highly preferred indications
invention) include the assays	include inflammation and
disclosed in Forrer et al., Biol	inflammatory disorders.
Chem 379(8-9):1101-1110	Highly preferred indications
(1998); Gupta et al., Exp Cell	also include neoplastic
Res 247(2): 495-504 (1999);	diseases (e.g., leukemia,
Kyriakis JM, Biochem Soc	lymphoma, and/or as described
Symp 64:29-48 (1999); Chang	below under
and Karin, Nature	"Hyperproliferative
410(6824):37-40 (2001); and	Disorders"). Highly preferred
Cobb MH, Prog Biophys Mol	indications include neoplasms
Biol 71(3-4):479-500 (1999);	and cancers, such as, leukemia,
the contents of each of which	lymphoma, prostate, breast,
are herein incorporated by	lung, colon, pancreatic,
 reference in its entirety. T	esophageal, stomach, brain,
cells that may be used	liver, and urinary cancer. Other
according to these assays are	preferred indications include
 publicly available (e.g.,	benign dysproliferative
through the ATCC).	disorders and pre-neoplastic
Exemplary mouse T cells that	conditions, such as, for
may be used according to these	example, hyperplasia,
assays include the CTLL cell	metaplasia, and/or dysplasia.
line, which is an IL-2	Preferred indications include
dependent suspension-culture	arthritis, asthma, AIDS,
cell line with cytotoxic	allergy, anemia, pancytopenia,

				activity.	leukopenia, thrombocytopenia, Hodgkin"s disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt"s lymphoma, granulomatous disease, inflammatory bowel disease, sepsis, psoriasis, suppression of immune reactions to transplanted organs and tissues, endocarditis, meningitis, and Lyme Disease.
146	HE2NV57	1094	Insulin Secretion	Assays for measuring secretion of insulin are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to stimulate insulin secretion. For example, insulin secretion is measured by FMAT using anti-rat insulin antibodies. Insulin secretion from pancreatic beta cells is upregulated by glucose and also by certain proteins/peptides, and disregulation is a key component in diabetes.	A highly preferred indication is diabetes mellitus. An additional highly preferred indication associated with diabetes (e.g., diabetic retinopathy, diabetic nephropathy, kidney disease (e.g., renal failure, nephropathy and/or other diseases and disorders as described in the "Renal Disorders" section below), diabetic neuropathy, nerve disease and nerve damage (e.g., due to diabetic neuropathy), blood vessel blockage, heart disease, stroke, impotence (e.g., due to diabetic neuropathy or blood vessel

Exemplary assays that may be	blockage), seizures, mental
used or routinely modified to	confusion, drowsiness,
test for stimulation of insulin	nonketotic hyperglycemic-
secretion (from pancreatic	hyperosmolar coma,
cells) by polypeptides of the	cardiovascular disease (e.g.,
invention (including antibodies	heart disease, atherosclerosis,
and agonists or antagonists of	microvascular disease,
 the invention) include assays	hypertension, stroke, and other
disclosed in: Shimizu, H., et	diseases and disorders as
al., Endocr J, 47(3):261-9	described in the
 (2000); Salapatek, A.M., et al.,	"Cardiovascular Disorders"
Mol Endocrinol, 13(8):1305-	section below), dyslipidemia,
17 (1999); Filipsson, K., et al.,	endocrine disorders (as
Ann N Y Acad Sci, 865:441-4	described in the "Endocrine
(1998); Olson, L.K., et al., J	Disorders" section below),
Biol Chem, 271(28):16544-52	neuropathy, vision impairment
(1996); and, Miraglia S et. al.,	(e.g., diabetic retinopathy and
Journal of Biomolecular	blindness), ulcers and impaired
Screening, 4:193-204 (1999),	wound healing, and infection
the contents of each of which	(e.g., infectious diseases and
is herein incorporated by	disorders as described in the
reference in its entirety.	"Infectious Diseases" section
Pancreatic cells that may be	below, especially of the
used according to these assays	urinary tract and skin), carpal
are publicly available (e.g.,	tunnel syndrome and
through the ATCC) and/or	Dupuytren's contracture).
may be routinely generated.	An additional highly preferred
Exemplary pancreatic cells that	indication is obesity and/or
may be used according to these	complications associated with
assays include HITT15 Cells.	obesity. Additional highly
HITT15 are an adherent	preferred indications include

epithelial cell line established from Syrian hamster islet cells transformed with SV40. These cells express glucagon, somatostatin, and glucocorticoid receptors. The cells secrete insulin, which is stimulated by glucose and glucagon and suppressed by somatostatin or glucocorticoids. ATTC# CRL-177 Refs: Lord and Ashcroft. Biochem. J. 219: 547-551; Santerre et al. Proc. Natl. Acad. Sci. USA 78: 4339-4343, 1981.		IL-6 FMAT. IL-6 is produced by T cells and has strong embodiment of the invention effects on B cells. IL-6 participates in IL-4 induced lgE production and increases IgA production (IgA plays a role in mucosal immunity).  IL-6 induces cytotoxic T cells. Deregulated expression of IL-6 has been linked to autoimmune disease, plasmacytomas, and chronic of mucosal immunity. Highly preferred indication is the stimulation or enhancement of mucosal immunity. Highly
	TNFa in Human T-cell 293T	Production of IL-6
	1094	1095
	HE2NV57	HE2PD49
	146	147

		Assays for imminomodulatory	blood disorders (e.g.
		and differentiation forth	Jerrita 11.1
		and differentiation factor	described below under
		proteins produced by a large	"Immune Activity", "Blood-
-		variety of cells where the	Related Disorders", and/or
		expression level is strongly	"Cardiovascular Disorders"),
		regulated by cytokines, growth	and infection (e.g., as
		factors, and hormones are well	described below under
		known in the art and may be	"Infectious Disease"). Highly
		used or routinely modified to	preferred indications include
		assess the ability of	autoimmune diseases (e.g.,
		polypeptides of the invention	rheumatoid arthritis, systemic
		(including antibodies and	lupus erythematosis, multiple
		agonists or antagonists of the	sclerosis and/or as described
		invention) to mediate	below) and
		immunomodulation and	immunodeficiencies (e.g., as
		differentiation and modulate T	described below). Highly
		cell proliferation and function.	preferred indications also
,		Exemplary assays that test for	include boosting a B cell-
		immunomodulatory proteins	mediated immune response
		evaluate the production of	and alternatively suppressing a
		cytokines, such as IL-6, and	B cell-mediated immune
		the stimulation and	response. Highly preferred
		upregulation of T cell	indications include
		proliferation and functional	inflammation and
		activities. Such assays that	inflammatory
		may be used or routinely	disorders.Additional highly
		modified to test	preferred indications include
		immunomodulatory and	asthma and allergy. Highly
	,	diffferentiation activity of	preferred indications include
		polypeptides of the invention	neoplastic diseases (e.g.,
***************************************		(including antibodies and	myeloma, plasmacytoma,

		agonists or antagonists of the	leukemia, lymphoma,
		invention) include assays	melanoma, and/or as described
		disclosed in Miraglia et al., J	below under
		Biomolecular Screening 4:193-	"Hyperproliferative
		204(1999); Rowland et al.,	Disorders"). Highly preferred
		"Lymphocytes: a practical	indications include neoplasms
		approach" Chapter 6:138-160	and cancers, such as, myeloma,
		(2000); and Verhasselt et al., J	plasmacytoma, leukemia,
		Immunol 158:2919-2925	lymphoma, melanoma, and
		(1997), the contents of each of	prostate, breast, lung, colon,
		which are herein incorporated	pancreatic, esophageal,
		by reference in its entirety.	stomach, brain, liver and
		Human dendritic cells that may	urinary cancer. Other preferred
-	- nu t-u-	be used according to these	indications include benign
		assays may be isolated using	dysproliferative disorders and
		techniques disclosed herein or	pre-neoplastic conditions, such
		otherwise known in the art.	as, for example, hyperplasia,
		Human dendritic cells are	metaplasia, and/or dysplasia.
		antigen presenting cells in	Preferred indications include
		suspension culture, which,	anemia, pancytopenia,
		when activated by antigen	leukopenia, thrombocytopenia,
	-	and/or cytokines, initiate and	Hodgkin's disease, acute
		upregulate T cell proliferation	lymphocytic anemia (ALL),
		and functional activities.	multiple myeloma, Burkitt's
			lymphoma, arthritis, AIDS,
			granulomatous disease,
			inflammatory bowel disease,
			sepsis, neutropenia,
			neutrophilia, psoriasis,
			suppression of immune
		_	reactions to transplanted

				HB-8065). See Knowles et al.,	
			-	science, 209:49/-9 (1980), the contents of which are herein	
		- Tapicker		incorporated by reference in its	
				entirety.	
149	HE6EU50	1097	CD69 in Human T		
	HE6EU50	1097	IL-2 in Human T-		
149			cell 293T		
	HE6EU50	1097	Activation of	Assays for the activation of	Highly preferred indications
149			transcription	transcription through the	include blood disorders (e.g.,
-113 - 34			through NFAT	Nuclear Factor of Activated T	as described below under
			response in immune	cells (NFAT) response element	"Immune Activity", "Blood-
			cells (such as T-	are well-known in the art and	Related Disorders", and/or
			cells).	may be used or routinely	"Cardiovascular Disorders").
				modified to assess the ability	Highly preferred indications
				of polypeptides of the	include autoimmune diseases
				invention (including antibodies	(e.g., rheumatoid arthritis,
				and agonists or antagonists of	systemic lupus erythematosis,
				the invention) to regulate	multiple sclerosis and/or as
				NFAT transcription factors and	described below),
				modulate expression of genes	immunodeficiencies (e.g., as
				involved in	described below), boosting a T
				immunomodulatory functions.	cell-mediated immune
				Exemplary assays for	response, and suppressing a T
				transcription through the	cell-mediated immune
				NFAT response element that	response. Additional highly
				may be used or routinely	preferred indications include
				modified to test NFAT-	inflammation and
				response element activity of	inflammatory disorders. An
				polypeptides of the invention	additional highly preferred

(including antibodies and	indication is infection (e.g., an
agonists or antagonists of the	infectious disease as described
invention) include assays	below under "Infectious
disclosed in Berger et al., Gene	Disease"). Preferred
66:1-10 (1998); Cullen and	indications include neoplastic
Malm, Methods in Enzymol	diseases (e.g., leukemia,
216:362-368 (1992); Henthorn	lymphoma, and/or as described
et al., Proc Natl Acad Sci USA	below under
85:6342-6346 (1988); Serfling	"Hyperproliferative
et al., Biochim Biophys Acta	Disorders"). Preferred
1498(1):1-18 (2000); De Boer	indications include neoplasms
et al., Int J Biochem Cell Biol	and cancers, such as, for
31(10):1221-1236 (1999);	example, leukemia, lymphoma,
Fraser et al., Eur J Immunol	and prostate, breast, lung,
29(3):838-844 (1999); and	colon, pancreatic, esophageal,
Yeseen et al., J Biol Chem	stomach, brain, liver and
268(19):14285-14293 (1993),	urinary cancer. Other preferred
the contents of each of which	indications include benign
are herein incorporated by	dysproliferative disorders and
reference in its entirety. T	pre-neoplastic conditions, such
cells that may be used	as, for example, hyperplasia,
according to these assays are	metaplasia, and/or dysplasia.
publicly available (e.g.,	Preferred indications also
through the ATCC).	include anemia, pancytopenia,
Exemplary human T cells that	leukopenia, thrombocytopenia,
 may be used according to these	Hodgkin's disease, acute
assays include the JURKAT	lymphocytic anemia (ALL),
cell line, which is a suspension	plasmacytomas, multiple
culture of leukemia cells that	myeloma, Burkitt's lymphoma,
 produce IL-2 when stimulated.	arthritis, AIDS, granulomatous
	disease, inflammatory bowel

disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, asthma and allergy.		Highly preferred indications	include neoplastic diseases	(e.g., leukemia, lymphoma,	and/or as described below	under "Hyperproliferative	Disorders"). Highly preferred	indications include neoplasms	and cancers, such as, for	s example, leukemia, lymphoma				Hodgkin's disease),	melanoma, and prostate,	breast, lung, colon, pancreatic,	esophageal, stomach, brain,	liver and urinary cancer. Other	preferred indications include	benign dysproliferative	
		Assays for the activation of	transcription through the	Gamma Interferon Activation	Site (GAS) response element	are well-known in the art and	may be used or routinely	modified to assess the ability	of polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) to regulate	STAT transcription factors and	modulate gene expression	involved in a wide variety of	cell functions. Exemplary	assays for transcription	through the GAS response	element that may be used or	routinely modified to test	GAS-response element activity
	SEAP in Jurkat/IL4 promoter	Activation of	transcription	through GAS	response element in	immune cells (such	as T-cells).														
	1097	1097																			
	HE6EU50	HE6EU50																			
	149		149		_						-										

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conditions, such as, for	example, hyperplasia,	metaplasia, and/or dysplasia.	Preferred indications include	autoimmune diseases (e.g.,	rheumatoid arthritis, systemic	lupus erythematosis, multiple	sclerosis and/or as described	below), immunodeficiencies	(e.g., as described below),	boosting a T cell-mediated	immune response, and	suppressing a T cell-mediated	immune response. Additional	preferred indications include	inflammation and	inflammatory disorders.	Highly preferred indications	include blood disorders (e.g.,	as described below under	"Immune Activity", "Blood-	Related Disorders", and/or	"Cardiovascular Disorders"),	and infection (e.g., viral	infections, tuberculosis,	infections associated with	chronic granulomatosus	disease and malignant	osteoporosis, and/or an	infectious disease as described	1. 1. 1. 1. 1. 1. 1. 1. 1. 1. 1. 1. 1. 1
of polypeptides of the	Invention (including antibodies	and agonists or antagonists of	the invention) include assays	disclosed in Berger et al., Gene	66:1-10 (1998); Cullen and	Malm, Methods in Enzymol	216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA	85:6342-6346 (1988);	Matikainen et al., Blood	93(6):1980-1991 (1999); and	Henttinen et al., J Immunol	155(10):4582-4587 (1995), the	contents of each of which are	herein incorporated by	reference in its entirety.	Exemplary human T cells,	such as the MOLT4 cell line,	that may be used according to	these assays are publicly	available (e.g., through the	ATCC).								
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				Disease"). An additional
				preferred indication is
				idiopathic pulmonary fibrosis.
				Preferred indications include
				anemia, pancytopenia,
				leukopenia, thrombocytopenia,
				acute lymphocytic anemia
				(ALL), plasmacytomas,
				multiple myeloma, arthritis,
				AIDS, granulomatous disease,
				inflammatory bowel disease,
				sepsis, neutropenia,
				neutrophilia, psoriasis,
				suppression of immune
				reactions to transplanted
				organs and tissues,
				hemophilia, hypercoagulation,
				diabetes mellitus, endocarditis,
				meningitis, Lyme Disease, and
				asthma and allergy.
HE8DS15	1098	Activation of	Kinase assay. Kinase assays,	A highly preferred
		Adipocyte ERK	for example an Elk-1 kinase	embodiment of the invention
		Signaling Pathway	assay, for ERK signal	includes a method for
			transduction that regulate cell	stimulating adipocyte
			proliferation or differentiation	proliferation. An alternative
			are well known in the art and	highly preferred embodiment
			may be used or routinely	of the invention includes a
			modified to assess the ability	method for inhibiting
			of polypeptides of the	adipocyte proliferation. A
			invention (including antibodies	highly preferred embodiment
			and agonists or antagonists of	of the invention includes a

adipocyte differentiation. An alternative highly preferred embodiment of the invention	includes a method for inhibiting adipocyte differentiation. A highly	preferred embodiment of the invention includes a method	for stimulating (e.g., increasing) adipocyte	activation. An alternative highly preferred embodiment	of the invention includes a	activation of (e.g., decreasing)	and/or inactivating adipocytes.	Highly preferred indications	include endocrine disorders (e.g., as described below under	"Endocrine Disorders").	Highly preferred indications	also include neoplastic	diseases (e.g., lipomas,	liposarcomas, and/or as	described below under	"Hyperproliferative	Disorders"). Preferred	indications include blood	disorders (e.g., hypertension,	congestive heart failure, blood
the invention) to promote or inhibit cell proliferation, activation, and differentiation. Exemplary assays for FRK	kinase activity that may be used or routinely modified to test ERK kinase-induced	activity of polypeptides of the invention (including antibodies	and agonists or antagonists of the invention) include the	assays disclosed in Forrer et al., Biol Chem 379(8-9):1101-	1110 (1998); Le Marchand-	Brustel Y, Exp Clin Endocrinol Diabetes	107(2):126-132 (1999);	Kyriakis JM, Biochem Soc	Symp 64:29-48 (1999); Chang   and Karin, Nature	410(6824):37-40 (2001); and	Cobb MH, Prog Biophys Mol	Biol 71(3-4):479-500 (1999);	the contents of each of which	are herein incorporated by	reference in its entirety.	Mouse adipocyte cells that	may be used according to these	assays are publicly available	(e.g., through the ATCC).	Exemplary mouse adipocyte
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blockage, heart disease, stroke,	impotence (e.g., due to diabetic	neuropathy or blood vessel	blockage), seizures, mental	confusion, drowsiness,	nonketotic hyperglycemic-	hyperosmolar coma,	cardiovascular disease (e.g.,	heart disease, atherosclerosis,	microvascular disease,	hypertension, stroke, and other	diseases and disorders as	described in the	"Cardiovascular Disorders"	section below), dyslipidemia,	endocrine disorders (as	described in the "Endocrine	Disorders" section below),	neuropathy, vision impairment	(e.g., diabetic retinopathy and	blindness), ulcers and impaired	wound healing, infection (e.g.,	infectious diseases and	disorders as described in the	"Infectious Diseases" section	below (particularly of the	urinary tract and skin). An	additional highly preferred	indication is obesity and/or	complications associated with	obesity. Additional highly
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preferred indications include	weight loss or alternatively,	weight gain. Additional	highly preferred indications are	complications associated with	insulin resistance.	Additional highly preferred	indications are disorders of the	musculoskeletal systems	including myopathies,	muscular dystrophy, and/or as	described herein.	Additional highly preferred	indications include,	hypertension, coronary artery	disease, dyslipidemia,	gallstones, osteoarthritis,	degenerative arthritis, eating	disorders, fibrosis, cachexia,	and kidney diseases or	disorders. Preferred	indications include neoplasms	and cancer, such as,	lymphoma, leukemia and	breast, colon, and kidney	cancer. Additional preferred	indications include melanoma,	prostate, lung, pancreatic,	esophageal, stomach, brain,	liver, and urinary cancer.	Highly preferred indications
					-																									

					include linomas and
					liposarcomas. Other preferred
	12.0				indications include benign
					dysproliferative disorders and
					pre-neoplastic conditions, such
					as, for example, hyperplasia,
					metaplasia, and/or dysplasia.
	HE8DS15	1098	Regulation of	Assays for the regulation of	A highly preferred
150			transcription of	transcription of Malic Enzyme	indication is diabetes mellitus.
			Malic Enzyme in	are well-known in the art and	An additional highly preferred
			adipocytes	may be used or routinely	indication is a complication
				modified to assess the ability	associated with diabetes (e.g.,
				of polypeptides of the	diabetic retinopathy, diabetic
7271				invention (including antibodies	nephropathy, kidney disease
	· · · · · · · · · · · · · · · · · · ·			and agonists or antagonists of	(e.g., renal failure,
				the invention) to regulate	nephropathy and/or other
				transcription of Malic Enzyme,	diseases and disorders as
				a key enzyme in lipogenesis.	described in the "Renal
				Malic enzyme is involved in	Disorders" section below),
				lipogenesisand its expression is	diabetic neuropathy, nerve
				stimulted by insulin. ME	disease and nerve damage
				promoter contains two direct	(e.g., due to diabetic
				repeat (DR1)- like elements	neuropathy), blood vessel
·				MEp and MEd identified as	blockage, heart disease, stroke,
				putative PPAR response	impotence (e.g., due to diabetic
	-			elements. ME promoter may	neuropathy or blood vessel
				also responds to AP1 and other	blockage), seizures, mental
				transcription factors.	confusion, drowsiness,
				Exemplary assays that may be	nonketotic hyperglycemic-
				used or routinely modified to	hyperosmolar coma,
			The state of the s	test for regulation of	cardiovascular disease (e.g.,

transcription of Malic Enzyme	heart disease, atherosclerosis,
	microvascular disease,
polypeptides of the invention	hypertension, stroke, and other
(including antibodies and	diseases and disorders as
agonists or antagonists of the	described in the
invention) include assays	"Cardiovascular Disorders"
disclosed in: Streeper, R.S., et	section below), dyslipidemia,
al., Mol Endocrinol,	endocrine disorders (as
12(11):1778-91 (1998);	described in the "Endocrine
Garcia-Jimenez, C., et al., Mol	Disorders" section below),
Endocrinol, 8(10):1361-9	neuropathy, vision impairment
(1994); Barroso, I., et al., J	(e.g., diabetic retinopathy and
Biol Chem, 274(25):17997-	blindness), ulcers and impaired
8004 (1999); Ijpenberg, A., et	wound healing, and infection
al., J Biol Chem,	(e.g., infectious diseases and
272(32):20108-20117 (1997);	disorders as described in the
Berger, et al., Gene 66:1-10	"Infectious Diseases" section
(1988); and, Cullen, B., et al.,	below, especially of the
Methods in Enzymol.	urinary tract and skin), carpal
216:362–368 (1992), the	tunnel syndrome and
contents of each of which is	Dupuytren's contracture).
herein incorporated by	An additional highly preferred
 reference in its entirety.	indication is obesity and/or
Hepatocytes that may be used	complications associated with
according to these assays are	obesity. Additional highly
publicly available (e.g.,	preferred indications include
through the ATCC) and/or	weight loss or alternatively,
may be routinely generated.	weight gain. Aditional
Exemplary hepatocytes that	highly preferred indications are
may be used according to these	complications associated with
assays includes the H4IIE rat	insulin resistance.

				liver hepatoma cell line.	
	HE8DS15	1098	Inhibition of	Reporter Assay: construct	
150			squalene synthetase	contains regulatory and coding	
			gene transcription.	sequence of squalene	
				synthetase, the first specific	
				enzyme in the cholesterol	
				biosynthetic pathway. See	
				Jiang, et al., J. Biol. Chem.	
				268:12818-128241(993), the	
				contents of which are herein	
				incorporated by reference in its	
				entirety. Cells were treated	
				with SID supernatants, and	
				SEAP activity was measured	
				after 72 hours. HepG2 is a	
				human hepatocellular	
				carcinoma cell line (ATCC	
				HB-8065). See Knowles et al.,	
				Science. 209:497-9 (1980), the	
				contents of which are herein	
				incorporated by reference in its	
				entirety.	
	HE8MH91	1099	Activation of	Assays for the activation of	Preferred embodiments of the
151			transcription	transcription through the	invention include using
			through NFKB	NFKB response element are	polypeptides of the invention
			response element in	well-known in the art and may	(or antibodies, agonists, or
			immune cells (such	be used or routinely modified	antagonists thereof) in
			as B-cells).	to assess the ability of	detection, diagnosis,
				polypeptides of the invention	prevention, and/or treatment of
				(including antibodies and	Cancer, Autoimmunity,
				agonists or antagonists of the	Allergy and Asthma

invention) to regulate NFKB transcription factors and modulate expression of immunomodulatory genes.	Exemplary assays for transcription through the NFKB response element that may be used or rountinely modified to test NFKB.	response element activity of polypeptides of the invention (including antibodies and	agonists or antagonists of the invention) include assays disclosed in: Gri G, et al., Biol Chem, 273(11):6431-6438	(1998); Pyatt DW, et al., Cell Biol Toxicol 2000;16(1):41-51 (2000); Berger et al., Gene 66:1-10 (1998); Cullen and	Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Valle	Blazquez et al, Immunology 90(3):455-460 (1997); Aramburau et al., J Exp Med 82(3):801-810 (1995); and	Fraser et al., 29(3):838-844 (1999), the contents of each of which are herein incorporated

by reference in its entirety.  Immune cells that may be used according to these assays are publicly available (e.g., through the ATCC).  Exemplary immune cells that may be used according to these assays include the Reh B-cell line.		4 IL-4 FMAT. Assays for A highly preferred immunomodulatory proteins embodiment of the invention		stimulate B cells, T cells, stimulating (e.g., increasing)	Ils	and promote polarization of highly preferred embodiment	<u>.</u>	well known in the art and may method for inhibiting (e.g.,	be used or routinely modified reducing) IL-4 production.	to assess the ability of A highly preferred indication	tion	(including antibodies and preferred indication includes	the	invention) to mediate indication includes rhinitis.	immunomodulation, stimulate   Additional highly preferred	immune cells, modulate indications include	immune cell polarization, inflammation and	and/or mediate humoral or inflammatory disorders.	cell-mediated immunity. Highly preferred indications	
	IgG in Human B cells SAC	Production of IL-4																		
	1100	1100																	<u>.</u>	
	HE8QV67	HE8QV67		<u> </u>																
	152	152	10T									49-00	_							

ımi	immunomodulatory proteins	(e.g., leukemia, lymphoma,
ense ense	evaluate the production of	melanoma, and/or as described
	cytokines, such as IL-4, and	below under
the	the stimulation of immune	"Hyperproliferative
cel cel	cells, such as B cells, T cells,	Disorders"). Preferred
ma	macrophages and mast cells.	indications include neoplasms
ns   Riversity   Since	Such assays that may be used	and cancers, such as, for
OL 1	or routinely modified to test	example, leukemia, lymphoma,
TIII.	immunomodulatory activity of	melanoma, and prostate,
lod	polypeptides of the invention	breast, lung, colon, pancreatic,
(in	(including antibodies and	esophageal, stomach, brain,
agc	agonists or antagonists of the	liver and urinary cancer. Other
nii	invention) include the assays	preferred indications include
dis dis	disclosed in Miraglia et al., J	benign dysproliferative
Bic Bic	Biomolecular Screening 4:193-	disorders and pre-neoplastic
707	204 (1999); Rowland et al.,	conditions, such as, for
<u></u>	"Lymphocytes: a practical	example, hyperplasia,
apr	approach" Chapter 6:138-160	metaplasia, and/or dysplasia.
	(2000); Gonzalez et al., J Clin	Preferred indications include
Lal	Lab Anal 8(5):277-283 (1194);	blood disorders (e.g., as
Ys	Yssel et al., Res Immunol	described below under
144	144(8):610-616 (1993); Bagley	"Immune Activity", "Blood-
et a	et al., Nat Immunol 1(3):257-	Related Disorders", and/or
261	261 (2000); and van der Graaff	"Cardiovascular Disorders").
et a	et al., Rheumatology (Oxford)	Preferred indications include
38(	38(3):214-220 (1999), the	autoimmune diseases (e.g.,
COL	contents of each of which are	rheumatoid arthritis, systemic
her	herein incorporated by	lupus erythematosis, multiple
refe	reference in its entirety.	sclerosis and/or as described
Hu Hu	Human T cells that may be	below) and
nse	used according to these assays	immunodeficiencies (e.g., as

***				may be isolated using	described below). Preferred
				techniques disclosed herein or	e ar
				otherwise known in the art.	pancytopenia, leukopenia,
				Human T cells are primary	thrombocytopenia, Hodgkin's
				human lymphocytes that	disease, acute lymphocytic
				mature in the thymus and	anemia (ALL),
				express a T cell receptor and	plasmacytomas, multiple
				CD3, CD4, or CD8. These	myeloma, Burkitt's lymphoma,
				cells mediate humoral or cell-	arthritis, AIDS, granulomatous
				mediated immunity and may	disease, inflammatory bowel
				be preactivated to enhance	disease, sepsis, neutropenia,
				responsiveness to	neutrophilia, psoriasis,
				immunomodulatory factors.	suppression of immune
			•		reactions to transplanted
					organs and tissues,
	-				hemophilia, hypercoagulation,
					diabetes mellitus, endocarditis,
					meningitis, and Lyme Disease.
					An additonal preferred
					indication is infection (e.g., an
					infectious disease as described
					below under "Infectious
					Disease").
153	HE9BK23	1101	IgG in Human B		
133			cells SAC	The state of the s	
	HE9BK23	1101	Activation of	Assays for the activation of	Highly preferred indications
153	· ·		transcription	transcription through the	include inflammation and
			through NFKB	NFKB response element are	inflammatory disorders.
			response element in	well-known in the art and may	Highly preferred indications
			immune cells (such	be used or routinely modified	include blood disorders (e.g.,
			as T-cells).	to assess the ability of	as described below under

			polypeptides of the invention	"Immune Activity", "Blood-
			(including antibodies and	Related Disorders", and/or
			agonists or antagonists of the	"Cardiovascular Disorders").
			invention) to regulate NFKB	Highly preferred indications
_			transcription factors and	include autoimmune diseases
			modulate expression of	(e.g., rheumatoid arthritis,
			immunomodulatory genes.	systemic lupus erythematosis,
	-11		Exemplary assays for	multiple sclerosis and/or as
			transcription through the	described below), and
			NFKB response element that	immunodeficiencies (e.g., as
			may be used or rountinely	described below). An
			modified to test NFKB-	additional highly preferred
1203			response element activity of	indication is infection (e.g.,
			polypeptides of the invention	AIDS, and/or an infectious
			(including antibodies and	disease as described below
•		,	agonists or antagonists of the	under "Infectious Disease").
			invention) include assays	Highly preferred indications
			disclosed in Berger et al., Gene	include neoplastic diseases
			66:1-10 (1998); Cullen and	(e.g., melanoma, leukemia,
			Malm, Methods in Enzymol	lymphoma, and/or as described
		•	216:362-368 (1992); Henthorn	below under
			et al., Proc Natl Acad Sci USA	"Hyperproliferative
			85:6342-6346 (1988); Black et	Disorders"). Highly preferred
			al., Virus Gnes 15(2):105-117	indications include neoplasms
			(1997); and Fraser et al.,	and cancers, such as, for
			29(3):838-844 (1999), the	example, melanoma, renal cell
			contents of each of which are	carcinoma, leukemia,
			herein incorporated by	lymphoma, and prostate,
			reference in its entirety.	breast, lung, colon, pancreatic,
			Exemplary human T cells,	esophageal, stomach, brain,
			such as the MOLT4, that may	liver and urinary cancer. Other

													_		
A highly preferred embodiment of the invention includes a method for	activating 1 cells. An alternative highly preferred embodiment of the invention includes a mathod for	includes a method for inhibiting the activation of and/or inactivating T cells. A highly preferred	embodiment of the invention includes a method for	stimulating (e.g., increasing) IL-2 production. An alternative	nignly preferred embodiment of the invention includes a	method for inhibiting (e.g., reducing) IL-2 production.	Additional highly preferred indications include	inflammation and inflammatory disorders	Highly preferred indications	include autoimmune diseases (e.g., rheumatoid arthritis,	systemic lupus erythematosis,	multiple sclerosis and/or as	immunodeficiencies (e.g., as	described below), boosting a T	cell-mediated immune
agonists or antagonists of the invention) to stimulate IL-2 expression in T cells.	transcription through the CD28 response element that may be	used or routinely modified to test CD28-response element activity of polypeptides of the invention (including antibodies	and agonists or antagonists of the invention) include assays	disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and	Malm, Methods in Enzymol 216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA 85:6342-6346 (1988);	McGuire and Iacobelli, J Immunol 159(3):1319-1327	(1997); Parra et al., J Immunol 166(4):2437-2443 (2001); and	Butscher et al., J Biol Chem	3(1):552-560 (1998), the contents of each of which are	herein incorporated by	reference in its entirety. T	according to these assays are	publicly available (e.g.,	through the ATCC).

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response, and suppressing a T cell-mediated immune	indications include neoplastic	diseases (e.g., melanoma, renal	nia,	lymphoma, and/or as described			Disorders"). Highly preferred	indications include neoplasms	or.	.; ie	renal	cell carcinoma (e.g., metastatic		leukemia, lymphoma (e.g., T	cell lymphoma), and prostate,	breast, lung, colon, pancreatic,	brain,	liver and urinary cancer. Other	preferred indications include	a)	lastic	<u>.</u>		metaplasia, and/or dysplasia.	A highly preferred indication	·:	AIDS, tuberculosis, infections	omator
response, and suppress cell-mediated immune	uny puv ide nec	elanor	cell carcinoma, leukemia,	or as d		ive	thly pr	ide nec	and cancers, such as, for	example, melanoma (e.g.,	metastatic melanoma), renal	e.g., m	oma),	oma (	and p	on, par	esophageal, stomach, brain,	cance	ions ii	benign dysproliferative	disorders and pre-neoplastic	conditions, such as, for	lasia,	or dys	ed ind	includes infection (e.g.,	sis, in	oranılı
and su	s inclu	s.g., m	oma, l	and,	ler	"Hyperproliferative	"). Hig	s inclu	rs, suc	nelan	melar	oma (	renal cell carcinoma),	lymph	ıoma),	ig, colo	ıl, ston	ırinary	indicat	sprolif	and pre	s, such	example, hyperplasia,	a, and/	referr	ıfectio	erculo	with s
onse, a-media	cation	ases (e	carcin	phoma	below under	perpro	orders'	cation	cancel	nple, 1	astatic	carcin	ıl cell (	emia,	lymph	ıst, lun	ohagea	r and u	erred i	ign dy	rders	ditions	mple, l	aplasia	ighly p	udes ii	S, tub	associated with granulomatous
***	ind:	dise	cell	lym	belc	(H,,	Disc	indi	and	exa	met	cell	rena	leuk	cell	prea	esol	live	pref	ben	diso	con	exal	met	Ah	incl	AIL	assc
s that these																												
T cells ding to	pensio	IL-4																										
accord	desays include the SOLL Colline, which is a suspension	-2 and	cells.																									
c used	hich i	e of IL	isive T																									
Exemplary human T cells that may be used according to these	assays line, w	culture of IL-2 and IL-4	responsive T cells.																									
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disease, and osteoporosis, and/or as described below under "Infectious Disease"). A	highly preferred indication is AIDS. Additional highly preferred indications include	suppression of immune reactions to transplanted	organs and/or tissues, uveitis, psoriasis, and tropical spastic	paraparesis. Preferred	disorders (e.g., as described	below under "Immune	Activity", "Blood-Related	Disorders", and/or	"Cardiovascular Disorders").	Preferred indications also	include anemia, pancytopenia,	leukopenia, thrombocytopenia,	Hodgkin's disease, acute	lymphocytic anemia (ALL),	plasmacytomas, multiple	myeloma, Burkitt's lymphoma,	arthritis, granulomatous	disease, inflammatory bowel	disease, sepsis, neutropenia,	neutrophilia, hemophilia,	hypercoagulation, diabetes	mellitus, endocarditis,	meningitis, Lyme Disease,
							16.0			- 29		<del></del>											
													-1-										- And
						-												-					

	3 3 3 3 3 3 3 3 3 3 3 3 3 3 3 3 3 3 3 3			10.00	asthma and allergy.
154	HE9CP41	1102	SEAP in ATP-3T3- L1		
	HE9CP41	1102	Activation of	Assays for the activation of	A preferred embodiment of
154			transcription	transcription through the	the invention includes a
			through serum	Serum Response Element	method for inhibiting (e.g.,
			response element in	(SRE) are well-known in the	reducing) TNF alpha
			immune cells (such	art and may be used or	production. An alternative
			as T-cells).	routinely modified to assess	preferred embodiment of the
				the ability of polypeptides of	invention includes a method
				the invention (including	for stimulating (e.g.,
				antibodies and agonists or	increasing) TNF alpha
				antagonists of the invention) to	production. Preferred
				regulate the serum response	indications include blood
				factors and modulate the	disorders (e.g., as described
				expression of genes involved	below under "Immune
				in growth. Exemplary assays	Activity", "Blood-Related
				for transcription through the	Disorders", and/or
				SRE that may be used or	"Cardiovascular Disorders"),
				routinely modified to test SRE	Highly preferred indications
				activity of the polypeptides of	include autoimmune diseases
				the invention (including	(e.g., rheumatoid arthritis,
				antibodies and agonists or	systemic lupus erythematosis,
		*****		antagonists of the invention)	Crohn"s disease, multiple
				include assays disclosed in	sclerosis and/or as described
				Berger et al., Gene 66:1-10	below), immunodeficiencies
				(1998); Cullen and Malm,	(e.g., as described below),
		<b></b>		Methods in Enzymol 216:362-	boosting a T cell-mediated
				368 (1992); Henthorn et al.,	immune response, and
				Proc Natl Acad Sci USA	suppressing a T cell-mediated
				85:6342-6346 (1988); and	immune response. Additional

					larbania thromboardania
					icanopeina, unomnocy topoma,
					Hodgkin's disease, acute
					lymphocytic anemia (ALL),
					plasmacytomas, multiple
			,		myeloma, Burkitt's lymphoma,
					arthritis, AIDS, granulomatous
					disease, inflammatory bowel
					disease, neutropenia,
					neutrophilia, psoriasis,
					suppression of immune
					reactions to transplanted
					organs and tissues,
					hemophilia, hypercoagulation,
					diabetes mellitus, endocarditis,
					meningitis, Lyme Disease,
					cardiac reperfusion injury, and
					asthma and allergy. An
					additional preferred indication
					is infection (e.g., an infectious
					disease as described below
					under "Infectious Disease").
154	HE9CP41	1102	IL-10 in Human T-cell 2B9		
	HE9CP41	1102	Caspase		
154			(+camptothecin) in		
			SW480		
	HE9DG49	1103	Activation of	Assays for the activation of	Highly preferred indications
155			transcription	transcription through the	include neoplastic diseases
			through GAS	Gamma Interferon Activation	(e.g., leukemia, lymphoma,
			response element in	Site (GAS) response element	and/or as described below
			immune cells (such	are well-known in the art and	under "Hyperproliferative

as T-cells).	may be used or routinely	Disorders"). Highly preferred
	modified to assess the ability	indications include neoplasms
	of polypeptides of the	and cancers, such as, for
	invention (including antibodies	example, leukemia, lymphoma
	and agonists or antagonists of	(e.g., T cell lymphoma,
	the invention) to regulate	Burkitt's lymphoma, non-
	STAT transcription factors and	Hodgkins lymphoma,
	modulate gene expression	Hodgkin"s disease),
	involved in a wide variety of	melanoma, and prostate,
	cell functions. Exemplary	breast, lung, colon, pancreatic,
 	assays for transcription	esophageal, stomach, brain,
	through the GAS response	liver and urinary cancer. Other
	element that may be used or	preferred indications include
	routinely modified to test	benign dysproliferative
 _	GAS-response element activity	disorders and pre-neoplastic
	of polypeptides of the	conditions, such as, for
-	invention (including antibodies	example, hyperplasia,
	and agonists or antagonists of	metaplasia, and/or dysplasia.
	the invention) include assays	Preferred indications include
	disclosed in Berger et al., Gene	autoimmune diseases (e.g.,
	66:1-10 (1998); Cullen and	rheumatoid arthritis, systemic
 	Malm, Methods in Enzymol	lupus erythematosis, multiple
	216:362-368 (1992); Henthorn	sclerosis and/or as described
	et al., Proc Natl Acad Sci USA	below), immunodeficiencies
	85:6342-6346 (1988);	(e.g., as described below),
	Matikainen et al., Blood	boosting a T cell-mediated
-	93(6):1980-1991 (1999); and	immune response, and
	Henttinen et al., J Immunol	suppressing a T cell-mediated
	155(10):4582-4587 (1995), the	immune response. Additional
	contents of each of which are	preferred indications include
	herein incorporated by	inflammation and

Highly preferred indications include blood disorders (e.g.,	"Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"), and infection (e.g., viral	infections, tuberculosis, infections associated with chronic granulomatosus disease and malignant osteoporosis, and/or an	infectious disease as described below under "Infectious Disease"). An additional	preferred indication is idiopathic pulmonary fibrosis. Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia,	acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease,	sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues,
Exemplary mouse T cells that may be used according to these	assays are publicly available (e.g., through the ATCC). Exemplary T cells that may be used according to these assays include the CTLL cell line,	which is a suspension culture of IL-2 dependent cytotoxic T cells.				
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hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, and asthma and allergy.				A highly preferred embodiment of the invention includes a method for stimulating adipocyte proliferation. An alternative highly preferred embodiment of the invention includes a method for inhibiting adipocyte proliferation. A highly preferred embodiment of the invention includes a method for stimulating adipocyte differentiation. An alternative highly preferred embodiment of the invention includes a method for inhibiting adipocyte differentiation. An alternative highly preferred embodiment of the invention includes a method for inhibiting adipocyte differentiation. A highly preferred embodiment of the invention includes a method
				Kinase assay. Kinase assays, for example an Elk-1 kinase assay, for ERK signal transduction that regulate cell proliferation or differentiation are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote or inhibit cell proliferation, activation, and differentiation. Exemplary assays for ERK kinase activity that may be used or routinely modified to test ERK kinase-induced activity of polypeptides of the invention (including antibodies
	IgG in Human B cells	Caspase (+paclitaxel) in SW480	SEAP in SW480	Activation of Adipocyte ERK Signaling Pathway
	1103	1103	1103	1104
	HE9DG49	HE9DG49	HE9DG49	НЕ9НУ07
	155	155	155	156

for stimulating (e.g., increasing) adipocyte	activation. An alternative	highly preferred embodiment	of the invention includes a	method for inhibiting the	activation of (e.g., decreasing)	and/or inactivating adipocytes.	Highly preferred indications	include endocrine disorders	(e.g., as described below under	"Endocrine Disorders").	Highly preferred indications	also include neoplastic	diseases (e.g., lipomas,	liposarcomas, and/or as	described below under	"Hyperproliferative	Disorders"). Preferred	indications include blood	disorders (e.g., hypertension,	congestive heart failure, blood	vessel blockage, heart disease,	stroke, impotence and/or as	described below under	"Immune Activity",	"Cardiovascular Disorders",	and/or "Blood-Related	Disorders"), immune disorders	(e.g., as described below under	"Immune Activity"), neural
and agonists or antagonists of the invention) include the	assays disclosed in Forrer et	al., Biol Chem 379(8-9):1101-	1110 (1998); Le Marchand-	Brustel Y, Exp Clin	Endocrinol Diabetes	107(2):126-132 (1999);	Kyriakis JM, Biochem Soc	Symp 64:29-48 (1999); Chang	and Karin, Nature	410(6824):37-40 (2001); and	Cobb MH, Prog Biophys Mol	Biol 71(3-4):479-500 (1999);	the contents of each of which	are herein incorporated by	reference in its entirety.	Mouse adipocyte cells that	may be used according to these	assays are publicly available	(e.g., through the ATCC).	Exemplary mouse adipocyte	cells that may be used	according to these assays	include 3T3-L1 cells. 3T3-L1	is an adherent mouse	preadipocyte cell line that is a	continuous substrain of 3T3	fibroblast cells developed	through clonal isolation and	undergo a pre-adipocyte to
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						<del></del>																		-			183		

disorders (e.g., as described below under "Neural Activity and Neurological Diseases"),	and infection (e.g., as	described below under "Infectious Disease").	A highly preferred indication	is diabetes mellitus. An	additional highly preferred	indication is a complication	associated with diabetes (e.g.,	diabetic retinopathy, diabetic	nephropathy, kidney disease	(e.g., renal failure,	nephropathy and/or other	diseases and disorders as	described in the "Renal	Disorders" section below),	diabetic neuropathy, nerve	disease and nerve damage	(e.g., due to diabetic	neuropathy), blood vessel	blockage, heart disease, stroke,	impotence (e.g., due to diabetic	neuropathy or blood vessel	blockage), seizures, mental	confusion, drowsiness,	nonketotic hyperglycemic-	hyperosmolar coma,	cardiovascular disease (e.g.,	heart disease, atherosclerosis,
adipose-like conversion under appropriate differentiation conditions known in the art.		***							- 4																		
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microvascular disease,	hypertension, stroke, and other	diseases and disorders as	described in the	"Cardiovascular Disorders"	section below), dyslipidemia,	endocrine disorders (as	described in the "Endocrine	Disorders" section below),	neuropathy, vision impairment	(e.g., diabetic retinopathy and	blindness), ulcers and impaired	wound healing, infection (e.g.,	infectious diseases and	disorders as described in the	"Infectious Diseases" section	below (particularly of the	urinary tract and skin). An	additional highly preferred	indication is obesity and/or	complications associated with	obesity. Additional highly	preferred indications include	weight loss or alternatively,	weight gain. Additional	highly preferred indications are	complications associated with	insulin resistance.	Additional highly preferred	indications are disorders of the	musculoskeletal systems
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					illusculai dysuopily, alid/of as
					described nerein.
					Additional highly preferred
					indications include,
					hypertension, coronary artery
					disease, dyslipidemia,
					gallstones, osteoarthritis,
					degenerative arthritis, eating
					disorders, fibrosis, cachexia,
					and kidney diseases or
					disorders. Preferred
					indications include neoplasms
	•				and cancer, such as,
					lymphoma, leukemia and
					breast, colon, and kidney
					cancer. Additional preferred
					indications include melanoma,
					prostate, lung, pancreatic,
					esophageal, stomach, brain,
					liver, and urinary cancer.
					Highly preferred indications
					include lipomas and
					liposarcomas. Other preferred
					indications include benign
					dysproliferative disorders and
					pre-neoplastic conditions, such
					as, for example, hyperplasia,
					metaplasia, and/or dysplasia.
	HE9HY07	1104	Regulation of	Assays for the regulation of	A highly preferred
156	,		transcription	transcription through the FAS	indication is diabetes mellitus.

through the FAS	promoter element are well-	An additional highly preferred
promoter element	known in the art and may be	indication is a complication
 in hepatocytes	used or routinely modified to	associated with diabetes (e.g.,
	assess the ability of	diabetic retinopathy, diabetic
	polypeptides of the invention	nephropathy, kidney disease
	(including antibodies and	(e.g., renal failure,
	agonists or antagonists of the	nephropathy and/or other
	invention) to activate the FAS	diseases and disorders as
 	promoter element in a reporter	described in the "Renal
	construct and to regulate	Disorders" section below),
	transcription of FAS, a key	diabetic neuropathy, nerve
	enzyme for lipogenesis. FAS	disease and nerve damage
	promoter is regulated by many	(e.g., due to diabetic
	transcription factors including	neuropathy), blood vessel
	SREBP. Insulin increases FAS	blockage, heart disease, stroke,
	gene transcription in livers of	impotence (e.g., due to diabetic
	diabetic mice. This	neuropathy or blood vessel
	stimulation of transcription is	blockage), seizures, mental
	also somewhat glucose	confusion, drowsiness,
	dependent. Exemplary assays	nonketotic hyperglycemic-
	that may be used or routinely	hyperosmolar coma,
	modified to test for FAS	cardiovascular disease (e.g.,
	promoter element activity (in	heart disease, atherosclerosis,
	hepatocytes) by polypeptides	microvascular disease,
	of the invention (including	hypertension, stroke, and other
	antibodies and agonists or	diseases and disorders as
	antagonists of the invention)	described in the
	include assays disclosed in	"Cardiovascular Disorders"
	Xiong, S., et al., Proc Natl	section below), dyslipidemia,
	Acad Sci U.S.A., 97(8):3948-	endocrine disorders (as
	53 (2000); Roder, K., et al.,	described in the "Endocrine

				Eur J Biochem, 260(3):743-51	Disorders" section below).
				(1999); Oskouian B, et al.,	neuropathy, vision impairment
	***			Biochem J, 317 (Pt 1):257-65	(e.g., diabetic retinopathy and
				(1996); Berger, et al., Gene	blindness), ulcers and impaired
				66:1-10 (1988); and, Cullen,	wound healing, and infection
				B., et al., Methods in Enzymol.	(e.g., infectious diseases and
				216:362–368 (1992), the	disorders as described in the
				contents of each of which is	"Infectious Diseases" section
				herein incorporated by	below, especially of the
				reference in its entirety.	urinary tract and skin), carpal
				Hepatocytes that may be used	tunnel syndrome and
				according to these assays, such	Dupuytren's contracture).
				as H4IIE cells, are publicly	An additional highly preferred
				available (e.g., through the	indication is obesity and/or
				ATCC) and/or may be	complications associated with
				routinely generated.	obesity. Additional highly
				Exemplary hepatocytes that	preferred indications include
				may be used according to these	weight loss or alternatively,
				assays include rat liver	weight gain. Aditional
44				hepatoma cell line(s) inducible	highly preferred indications are
				with glucocorticoids, insulin,	complications associated with
				or cAMP derivatives.	insulin resistance.
157	HE9NN84	1105	SEAP in 293/ISRE		
	HE9NN84	1105	Activation of	Assays for the activation of	A highly preferred indication
157			transcription	transcription through the	is obesity and/or complications
			through cAMP	cAMP response element are	associated with obesity.
		-	response element	well-known in the art and may	Additional highly preferred
			(CRE) in pre-	be used or routinely modified	indications include weight loss
			adipocytes.	to assess the ability of	or alternatively, weight gain.
				polypeptides of the invention	An additional highly preferred

		(including antibodies and	indication is diabetes mellitus.
		agonists or antagonists of the	An additional highly preferred
		invention) to increase cAMP,	indication is a complication
		regulate CREB transcription	associated with diabetes (e.g.,
		factors, and modulate	diabetic retinopathy, diabetic
		expression of genes involved	nephropathy, kidney disease
		in a wide variety of cell	(e.g., renal failure,
		functions. For example, a	nephropathy and/or other
		3T3-L1/CRE reporter assay	diseases and disorders as
		may be used to identify factors	described in the "Renal
		that activate the cAMP	Disorders" section below),
	٠	signaling pathway. CREB	diabetic neuropathy, nerve
		plays a major role in	disease and nerve damage
		adipogenesis, and is involved	(e.g., due to diabetic
		in differentiation into	neuropathy), blood vessel
		adipocytes. CRE contains the	blockage, heart disease, stroke,
		binding sequence for the	impotence (e.g., due to diabetic
		transcription factor CREB	neuropathy or blood vessel
		(CRE binding protein).	blockage), seizures, mental
		Exemplary assays for	confusion, drowsiness,
		transcription through the	nonketotic hyperglycemic-
		cAMP response element that	hyperosmolar coma,
		may be used or routinely	cardiovascular disease (e.g.,
		modified to test cAMP-	heart disease, atherosclerosis,
	٠	response element activity of	microvascular disease,
		polypeptides of the invention	hypertension, stroke, and other
		(including antibodies and	diseases and disorders as
		agonists or antagonists of the	described in the
		invention) include assays	"Cardiovascular Disorders"
J		disclosed in Berger et al., Gene	section below), dyslipidemia,
		66:1-10 (1998); Cullen and	endocrine disorders (as

				Malm, Methods in Enzymol	described in the "Endocrine
				216:362-368 (1992); Henthorn	Disorders" section below),
				et al., Proc Natl Acad Sci USA	neuropathy, vision impairment
				85:6342-6346 (1988); Reusch	(e.g., diabetic retinopathy and
				et al., Mol Cell Biol	blindness), ulcers and impaired
				20(3):1008-1020 (2000); and	wound healing, and infection
	- 74			Klemm et al., J Biol Chem	(e.g., infectious diseases and
				273:917-923 (1998), the	disorders as described in the
				contents of each of which are	"Infectious Diseases" section
				herein incorporated by	below, especially of the
				reference in its entirety. Pre-	urinary tract and skin), carpal
- 10				adipocytes that may be used	tunnel syndrome and
				according to these assays are	Dupuytren's contracture).
				publicly available (e.g.,	Additional highly preferred
				through the ATCC) and/or	indications are complications
				may be routinely generated.	associated with insulin
		*****		Exemplary mouse adipocyte	resistance.
				cells that may be used	
				according to these assays	
				include 3T3-L1 cells. 3T3-L1	
				is an adherent mouse	
				preadipocyte cell line that is a	
				continuous substrain of 3T3	
				fibroblast cells developed	
				through clonal isolation and	
				undergo a pre-adipocyte to	
				adipose-like conversion under	
*****				appropriate differentiation	
				conditions known in the art.	
	HE9NN84	1105	Activation of	This reporter assay measures	Highly preferred indications
157			transcription	activation of the GATA-3	include allergy, asthma, and

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rhinitis. Additional preferred	indications include infection	(e.g., an infectious disease as	described below under	"Infectious Disease"), and	inflammation and	inflammatory disorders.	Preferred indications also	include blood disorders (e.g.,	as described below under	"Immune Activity", "Blood-	Related Disorders", and/or	"Cardiovascular Disorders").	Preferred indications include	autoimmune diseases (e.g.,	rheumatoid arthritis, systemic	lupus erythematosis, multiple	sclerosis and/or as described	below) and	immunodeficiencies (e.g., as	described below). Preferred	indications include neoplastic	diseases (e.g., leukemia,	lymphoma, melanoma,	prostate, breast, lung, colon,	pancreatic, esophageal,	stomach, brain, liver, and	urinary tract cancers and/or as	described below under	"Hyperproliferative	Disorders") Other preferred
signaling pathway in HMC-1	human mast cell line.	Activation of GATA-3 in mast	cells has been linked to	cytokine and chemokine	production. Assays for the	activation of transcription	through the GATA3 response	element are well-known in the	art and may be used or	routinely modified to assess	the ability of polypeptides of	the invention (including	antibodies and agonists or	antagonists of the invention) to	regulate GATA3 transcription	factors and modulate	expression of mast cell genes	important for immune response	development. Exemplary	assays for transcription	through the GATA3 response	element that may be used or	routinely modified to test	GATA3-response element	activity of polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) include assays	disclosed in Berger et al., Gene	66·1-10 (1998)· Cullen and
through GATA-3	response element in	immune cells (such	as mast cells).																											
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		A Committee of the Comm		Malm Methods in Enzymol	indications include henian
				716:362-368 (1992): Henthorn	dysproliferative disorders and
				210:302-308 (1//2), Heliuolii 24 al Diez Ned A = 4 C : 110 A	dyspromeranive disorders and
_				et al., Froc Natl Acad Sci USA	pre-neoplastic conditions, such
				85:6342-6346 (1988); Flavell	as, for example, hyperplasia,
				et al., Cold Spring Harb Symp	metaplasia, and/or dysplasia.
				Quant Biol 64:563-571 (1999);	Preferred indications include
				Rodriguez-Palmero et al., Eur	anemia, pancytopenia,
				J Immunol 29(12):3914-3924	leukopenia, thrombocytopenia,
				(1999); Zheng and Flavell,	leukemias, Hodgkin's disease,
				Cell 89(4):587-596 (1997); and	acute lymphocytic anemia
				Henderson et al., Mol Cell Biol	(ALL), plasmacytomas,
-	•			14(6):4286-4294 (1994), the	multiple myeloma, Burkitt's
				contents of each of which are	lymphoma, arthritis, AIDS,
				herein incorporated by	granulomatous disease,
				reference in its entirety. Mast	inflammatory bowel disease,
				cells that may be used	sepsis, neutropenia,
				according to these assays are	neutrophilia, psoriasis,
				publicly available (e.g.,	suppression of immune
				through the ATCC).	reactions to transplanted
				Exemplary human mast cells	organs and tissues, hemophilia,
				that may be used according to	hypercoagulation, diabetes
				these assays include the HMC-	mellitus, endocarditis,
				1 cell line, which is an	meningitis, and Lyme Disease.
				immature human mast cell line	
				established from the peripheral	
				blood of a patient with mast	
				cell leukemia, and exhibits	
				many characteristics of	
				immature mast cells.	
	HE9NN84	1105	Activation of	This reporter assay measures	Highly preferred indications
157	and the state of t		transcription	activation of the NFAT	include allergy, asthma, and

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rhinitis Additional preferred	indications include infection	(e.g., an infectious disease as	described below under	"Infectious Disease"), and	inflammation and	inflammatory disorders.	Preferred indications also	include blood disorders (e.g.,	as described below under	"Immune Activity", "Blood-	Related Disorders", and/or	"Cardiovascular Disorders").	Preferred indications include	autoimmune diseases (e.g.,	rheumatoid arthritis, systemic	lupus erythematosis, multiple	sclerosis and/or as described	below) and	immunodeficiencies (e.g., as	described below). Preferred	indications include neoplastic	diseases (e.g., leukemia,	lymphoma, melanoma,	prostate, breast, lung, colon,	pancreatic, esophageal,	stomach, brain, liver, and	urinary tract cancers and/or as	described below under	"Hyperproliferative	Disorders"). Other preferred
sionalino nathway in HMC-1	human mast cell line.	Activation of NFAT in mast	cells has been linked to	cytokine and chemokine	production. Assays for the	activation of transcription	through the Nuclear Factor of	Activated T cells (NFAT)	response element are well-	known in the art and may be	used or routinely modified to	assess the ability of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) to regulate NFAT	transcription factors and	modulate expression of genes	involved in	immunomodulatory functions.	Exemplary assays for	transcription through the	NFAT response element that	may be used or routinely	modified to test NFAT-	response element activity of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include assays
through NFAT	response element in	immune cells (such	as mast cells).																					A. A. A.						
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		disclosed in Berger et al. Gene	indications include henion
		66:1-10 (1998): Cullen and	dysproliferative disorders and
-		Malm, Methods in Enzymol	pre-neonlastic conditions such
		216:362-368 (1992); Henthorn	as, for example, hyperplasia.
-	<del></del>	et al., Proc Natl Acad Sci USA	metaplasia, and/or dysplasia.
		85:6342-6346 (1988); De Boer	Preferred indications include
		et al., Int J Biochem Cell Biol	anemia, pancytopenia,
		31(10):1221-1236 (1999); Ali	leukopenia, thrombocytopenia,
		et al., J Immunol	leukemias, Hodgkin's disease,
		165(12):7215-7223 (2000);	acute lymphocytic anemia
		Hutchinson and McCloskey, J	(ALL), plasmacytomas,
		Biol Chem 270(27):16333-	multiple myeloma, Burkitt's
		16338 (1995), and Turner et	lymphoma, arthritis, AIDS,
		al., J Exp Med 188:527-537	granulomatous disease,
		(1998), the contents of each of	inflammatory bowel disease,
		which are herein incorporated	sepsis, neutropenia,
		by reference in its entirety.	neutrophilia, psoriasis,
		Mast cells that may be used	suppression of immune
		according to these assays are	reactions to transplanted
		publicly available (e.g.,	organs and tissues, hemophilia,
		through the ATCC).	hypercoagulation, diabetes
		Exemplary human mast cells	mellitus, endocarditis,
		that may be used according to	meningitis, and Lyme Disease.
		these assays include the HMC-	
		1 cell line, which is an	
		immature human mast cell line	
•		established from the peripheral	
		blood of a patient with mast	
	-	cell leukemia, and exhibits	
		many characteristics of	
		immature mast cells.	

	TIPO CHILDO	70,00			and a control of the
158	HE90W20	1106	HLA-DK in Human T cells		
!	HE90W20	1106	Activation of	Kinase assay. Kinase assays,	Highly preferred indications
158			Skeletal Muscle	for examplek Elk-1 kinase	include endocrine disorders
			Cell ERK	assays, for ERK signal	(e.g., as described below under
			Signalling Pathway	transduction that regulate cell	"Endocrine Disorders") and
				proliferation or differentiation	disorders of the
				are well known in the art and	musculoskeletal system.
				may be used or routinely	Preferred indications include
				modified to assess the ability	neoplastic diseases (e.g., as
				of polypeptides of the	described below under
				invention (including antibodies	"Hyperproliferative
				and agonists or antagonists of	Disorders"), blood disorders
				the invention) to promote or	(e.g., as described below under
				inhibit cell proliferation,	"Immune Activity",
				activation, and differentiation.	"Cardiovascular Disorders",
				Exemplary assays for ERK	and/or "Blood-Related
				kinase activity that may be	Disorders"), immune disorders
				used or routinely modified to	(e.g., as described below under
				test ERK kinase-induced	"Immune Activity"), neural
			•	activity of polypeptides of the	disorders (e.g., as described
				invention (including antibodies	below under "Neural Activity
				and agonists or antagonists of	and Neurological Diseases"),
				the invention) include the	and infection (e.g., as
				assays disclosed in Forrer et	described below under
				al., Biol Chem 379(8-9):1101-	"Infectious Disease"). A
				1110 (1998); Le Marchand-	highly preferred indication is
				Brustel Y, Exp Clin	diabetes mellitus. An
			-	Endocrinol Diabetes	additional highly preferred
				107(2):126-132 (1999);	indication is a complication
				Kyriakis JM, Biochem Soc	associated with diabetes (e.g.,

	Symp 64:29-48 (1999); Chang	diabetic retinopathy, diabetic
	and Karin, Nature	nephropathy, kidney disease
40 (4.	410(6824):37-40 (2001); and	(e.g., renal failure,
	Cobb MH, Prog Biophys Mol	nephropathy and/or other
	Biol 71(3-4):479-500 (1999);	diseases and disorders as
	the contents of each of which	described in the "Renal
	are herein incorporated by	Disorders" section below),
	reference in its entirety. Rat	diabetic neuropathy, nerve
	myoblast cells that may be	disease and nerve damage
	used according to these assays	(e.g., due to diabetic
	are publicly available (e.g.,	neuropathy), blood vessel
	through the ATCC).	blockage, heart disease, stroke,
	Exemplary rat myoblast cells	impotence (e.g., due to diabetic
	that may be used according to	neuropathy or blood vessel
	these assays include L6 cells.	blockage), seizures, mental
	L6 is an adherent rat myoblast	confusion, drowsiness,
	cell line, isolated from primary	nonketotic hyperglycemic-
	cultures of rat thigh muscle,	hyperosmolar coma,
	that fuses to form	cardiovascular disease (e.g.,
	multinucleated myotubes and	heart disease, atherosclerosis,
	striated fibers after culture in	microvascular disease,
	differentiation media.	hypertension, stroke, and other
		diseases and disorders as
		described in the
		"Cardiovascular Disorders"
		section below), dyslipidemia,
		endocrine disorders (as
		described in the "Endocrine
		Disorders" section below),
		neuropathy, vision impairment
		(e.g., diabetic retinopathy and

					Lindana, ban amount (another)
					ominances), uncers and impaired
					wound healing, infection (e.g.,
					infectious diseases and
					disorders as described in the
					"Infectious Diseases" section
					below, especially of the
					urinary tract and skin), carpal
					tunnel syndrome and
					Dupuytren's contracture).
					An additional highly preferred
_	_				indication is obesity and/or
					complications associated with
		-			obesity. Additional highly
					preferred indications include
					weight loss or alternatively,
22			•		weight gain. Aditional
					highly preferred indications are
					complications associated with
					insulin resistance.
					Additonal highly preferred
					indications are disorders of the
					musculoskeletal systems
					including myopathies,
				- A day	muscular dystrophy, and/or as
					described herein.
					Additional highly preferred
					indications include: myopathy,
-					atrophy, congestive heart
					failure, cachexia, myxomas,
<del></del>					fibromas, congenital
					cardiovascular abnormalities.

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Disorders"). Highly preferred indications include neonlocus	and cancers, such as, for	example, melanoma, and	prostate, breast, lung, colon,	pancreatic, esophageal,	stomach, brain, liver and	urinary cancer. Other preferred	indications include benign	dysproliferative disorders and	pre-neoplastic conditions, such	as, for example, hyperplasia,	metaplasia, and/or dysplasia.	Preferred indications include	include inflammation and	inflammatory disorders.	•														
assays for transcription	element that may be used or	routinely modified to test	NFKB-response element	activity of polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) include assays	disclosed in: Kaltschmidt B, et	al., Oncogene, 18(21):3213-	3225 (1999); Beetz A, et al.,	Int J Radiat Biol, 76(11):1443-	1453 (2000); Berger et al.,	Gene 66:1-10 (1998); Cullen	and Malm, Methods in	Enzymol 216:362-368 (1992);	Henthorn et al., Proc Natl	Acad Sci USA 85:6342-6346	(1988); Valle Blazquez et al,	Immunology 90(3):455-460	(1997); Aramburau et al., J	Exp Med 82(3):801-810	(1995); and Fraser et al.,	29(3):838-844 (1999), the	contents of each of which are	herein incorporated by	reference in its entirety.	Epithelial cells that may be	used according to these assays	are publicly available (e.g.,
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0	Preferred indications include	described below under		Related Disorders", and/or	"Cardiovascular Disorders"),	and infection (e.g., an	infectious disease as described	below under "Infectious	Disease"). Preferred	indications include	autoimmune diseases (e.g.,	rheumatoid arthritis, systemic	lupus erythematosis, multiple	sclerosis and/or as described	below), immunodeficiencies	(e.g., as described below),	boosting a T cell-mediated	immune response, and	suppressing a T cell-mediated	immune response. Additional		inflammation and			include neonlastic discons
through the ATCC). Exemplary epithelial cells that may be used according to these assays include the HELA cell line.	Assays for the activation of transcription through the	cAMP response element are	well-known in the art and may	be used or routinely modified	to assess the ability of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) to increase cAMP	and regulate CREB	transcription factors, and	modulate expression of genes	involved in a wide variety of	cell functions. Exemplary	assays for transcription	through the cAMP response	element that may be used or	routinely modified to test	cAMP-response element	activity of polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) include assays	disclosed in Berger et al., Gene	66:1-10 (1998): Cullen and
	Activation of transcription	through cAMP	response element in	immune cells (such	as I-cells).			-																	
	1108				7-1																				
	HEAAR07																								
	160																								

			•
		Malm, Methods in Enzymol	(e.g., leukemia, lymphoma,
		216:362-368 (1992); Henthorn	and/or as described below
		et al., Proc Natl Acad Sci USA	under "Hyperproliferative
		85:6342-6346 (1988); Black et	Disorders"). Highly preferred
		al., Virus Genes 15(2):105-117	indications include neoplasms
		(1997); and Belkowski et al., J	and cancers, such as, for
		Immunol 161(2):659-665	example, leukemia, lymphoma
		(1998), the contents of each of	(e.g., T cell lymphoma,
		which are herein incorporated	Burkitt's lymphoma, non-
		by reference in its entirety. T	Hodgkins lymphoma,
		cells that may be used	Hodgkin"s disease),
		according to these assays are	melanoma, and prostate,
		publicly available (e.g.,	breast, lung, colon, pancreatic,
****		through the ATCC).	esophageal, stomach, brain,
		Exemplary mouse T cells that	liver and urinary cancer. Other
		may be used according to these	preferred indications include
		assays include the CTLL cell	benign dysproliferative
		line, which is a suspension	disorders and pre-neoplastic
		culture of IL-2 dependent	conditions, such as, for
	- 11	cytotoxic T cells.	example, hyperplasia,
			metaplasia, and/or dysplasia.
			Preferred indications include
			anemia, pancytopenia,
			leukopenia, thrombocytopenia,
			acute lymphocytic anemia
			(ALL), plasmacytomas,
			multiple myeloma, arthritis,
			AIDS, granulomatous disease,
			inflammatory bowel disease,
			sepsis, neutropenia,
			neutrophilia, psoriasis,

					suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation,
,					diabetes mellitus, endocarditis, meningitis, Lyme Disease, and asthma and allergy.
160	HEAAR07	1108	Hexosaminidase in RBL-2H3		
161	HEBAE88	1109	SEAP in 3T3L1		
	HEBAE88	1109	Activation of	Assays for the activation of	Preferred indications include
161			transcription	transcription through the	blood disorders (e.g., as
			through cAMP	cAMP response element are	described below under
			response element in	well-known in the art and may	"Immune Activity", "Blood-
			immune cells (such	be used or routinely modified	Related Disorders", and/or
			as T-cells).	to assess the ability of	"Cardiovascular Disorders"),
				polypeptides of the invention	and infection (e.g., an
				(including antibodies and	infectious disease as described
				agonists or antagonists of the	below under "Infectious
				invention) to increase cAMP	Disease"). Preferred
				and regulate CREB	indications include
	<u>.</u>			transcription factors, and	autoimmune diseases (e.g.,
				modulate expression of genes	rheumatoid arthritis, systemic
				involved in a wide variety of	lupus erythematosis, multiple
				cell functions. Exemplary	sclerosis and/or as described
				assays for transcription	below), immunodeficiencies
				through the cAMP response	(e.g., as described below),
				element that may be used or	boosting a T cell-mediated
				routinely modified to test	immune response, and
				cAMP-response element	suppressing a T cell-mediated

	activity of polypeptides of the	immune response. Additional
	invention (including antibodies	preferred indications include
	and agonists or antagonists of	inflammation and
	the invention) include assays	inflammatory disorders.
	disclosed in Berger et al., Gene	Highly preferred indications
	66:1-10 (1998); Cullen and	include neoplastic diseases
	Malm, Methods in Enzymol	(e.g., leukemia, lymphoma,
	216:362-368 (1992); Henthorn	and/or as described below
 	et al., Proc Natl Acad Sci USA	under "Hyperproliferative
	85:6342-6346 (1988); Black et	Disorders"). Highly preferred
	al., Virus Genes 15(2):105-117	indications include neoplasms
	(1997); and Belkowski et al., J	and cancers, such as, for
	Immunol 161(2):659-665	example, leukemia, lymphoma
	(1998), the contents of each of	(e.g., T cell lymphoma,
	which are herein incorporated	Burkitt's lymphoma, non-
	by reference in its entirety. T	Hodgkins lymphoma,
	cells that may be used	Hodgkin"s disease),
	according to these assays are	melanoma, and prostate,
	publicly available (e.g.,	breast, lung, colon, pancreatic,
	through the ATCC).	esophageal, stomach, brain,
 -	Exemplary mouse T cells that	liver and urinary cancer. Other
	may be used according to these	preferred indications include
	assays include the CTLL cell	benign dysproliferative
	line, which is a suspension	disorders and pre-neoplastic
	culture of IL-2 dependent	conditions, such as, for
	cytotoxic T cells.	example, hyperplasia,
		metaplasia, and/or dysplasia.
		Preferred indications include
		anemia, pancytopenia,
		leukopenia, thrombocytopenia,
,		acute lymphocytic anemia

(ALL), plasmacytomas, multiple myeloma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, and asthma and allergy.		Preferred embodiments of the invention include using polypeptides of the invention (or antibodies, agonists, or antagonists thereof) in detection, diagnosis, prevention, and/or treatment of asthma, allergy, hypersensitivity and inflammation.
		Caspase Apoptosis. Assays for caspase apoptosis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate caspase protease-mediated apoptosis in immune cells (such as, for example, in mast cells). Mast cells are found in connective and mucosal tissues throughout the body, and their activation via immunoglobulin E.
	SEAP in OE-33	Regulation of apoptosis of immune cells (such as mast cells).
	1109	1110
	HEBAE88	HEBBN36
	161	162

antigen, promoted by T helper cell type 2 cytokines, is an important component of allergic disease. Dysregulation of mast cell apoptosis may play a role in allergic disease and mast cell tumor survival.	Exemplary assays for caspase apoptosis that may be used or routinely modified to test capase apoptosis activity induced by polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include the assays disclosed in: Masuda A,	et al., J Biol Chem, 276(28):26107-26113 (2001); Yeatman CF 2nd, et al., J Exp Med, 192(8):1093-1103 (2000);Lee et al., FEBS Lett 485(2-3): 122-126 (2000); Nor et al., J Vasc Res 37(3): 209- 218 (2000); and Karsan and	Harlan, J Atheroscler Thromb 3(2): 75-80 (1996); the contents of each of which are herein incorporated by reference in its entirety. Immune cells that may be used according to these assays are

	g., corres)	ells that	g to these	ells such	nast cell	-	ion of Highly preferred indications				art and inflammatory disorders.	lely Additional highly preferred			-		ulate "Blood-Related Disorders"),	monly autoimmune diseases (e.g.,		riety of   lupus erythematosis, Crohn"s	plary disease, multiple sclerosis		onse immunodeficiencies (e.g., as			it activity response and, alternatively,		intibodies   mediated immune response.	onists of	3716336
	publicly available (e.g., through commercial sources)	Exemplary immune cells that	may be used according to these	assays include mast cells such	as the HMC human mast cell	line.	Assays for the activation of	transcription through the	Gamma Interferon Activation	ent in   Site (GAS) response element	(such   are well-known in the art and	). may be used or routinely	modified to assess the ability	of polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) to modulate	gene expression (commonly	via STAT transcription factors)	involved in a wide variety of	cell functions. Exemplary	assays for transcription	through the GAS response	element that may be used or	routinely modified to test	GAS-response element activity	of polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention include account
		-			V-11.		111 Activation of	transcription	through GAS	response element in	immune cells (such	as eosinophils).																310-		
190							HEBCM63																							
								163																						

disclosed in Berger et al., Gene	66:1-10 (1998); Cullen and	Malm, Methods in Enzymol	216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA	85:6342-6346 (1988);	Matikainen et al., Blood	93(6):1980-1991 (1999); and	Henttinen et al., J Immunol	155(10):4582-4587 (1995); the	contents of each of which are	herein incorporated by	reference in its entirety.	Moreover, exemplary assays	that may be used or routinely	modified to assess the ability	of polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) to activate or	inhibit activation of immune	cells include assays disclosed	and/or cited in: Mayumi M.,	"EoL-1, a human eosinophilic	cell line" Leuk Lymphoma;	Jun;7(3):243-50 (1992);	Bhattacharya S, "Granulocyte	macrophage colony-	stimulating factor and	interleukin-5 activate STAT5	and induce CIS1 mRNA in
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		A highly preferred embodiment of the invention includes a method for
human peripheral blood eosinophils" Am J Respir Cell Mol Biol; Mar;24(3):312-6 (2001); and, Du J, et al., "Engagement of the CrkL adapter in interleukin-5 signaling in eosinophils" J Biol Chem; Oct 20;275(42):33167-75 (2000); the contents of each of which are herein incorporated by reference in its entirety. Exemplary cells that may be used according to these assays include eosinophils. Eosinophils are a type of immune cell important in the late stage of allergic reactions; they are recruited to tissues and mediate the inflammtory response of late stage allergic reaction. Increases in GAS mediated transcription in eosinophils is typically a result of STAT activation, normally a direct consequence of interleukin or other cytokine	IL5 or GMCSF).	IFNgamma FMAT. IFNg plays a central role in the immune system and is considered to be
		Production of IFNgamma using a T cells
ı		1111
		НЕВСМ63
		163

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stimulating the production of IFNg. An alternative highly	preferred embodiment of the invention includes a method	for inhibiting the production of	IFNg. Highly preferred		disorders (e.g., as described	below under "Immune	Activity", "Blood-Related	Disorders", and/or	"Cardiovascular Disorders"),	and infection (e.g., viral	infections, tuberculosis,	infections associated with	chronic granulomatosus	disease and malignant	osteoporosis, and/or as	described below under	"Infectious Disease"). Highly	preferred indications include	autoimmune disease (e.g.,	rheumatoid arthritis, systemic	lupus erythematosis, multiple	sclerosis and/or as described	below), immunodeficiency	(e.g., as described below),	boosting a T cell-mediated	immune response, and	suppressing a T cell-mediated	immune response. Additional
a proinflammatory cytokine.  IFNg promotes TH1 and	inhibits 1 H2 differentiation; promotes IgG2a and inhibits	IgE secretion; induces	macrophage activation; and	increases MHC expression.	Assays for immunomodulatory	proteins produced by T cells	and NK cells that regulate a	variety of inflammatory	activities and inhibit TH2	helper cell functions are well	known in the art and may be	used or routinely modified to	assess the ability of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) to mediate	immunomodulation, regulate	inflammatory activities,	modulate TH2 helper cell	function, and/or mediate	humoral or cell-mediated	immunity. Exemplary assays	that test for	immunomodulatory proteins	evaluate the production of	cytokines, such as Interferon	gamma (IFNg), and the
	,																											
																	745											

acti	activation of T cells. Such	highly preferred indications
assi	assays that may be used or	include inflammation and
rou	routinely modified to test	inflammatory disorders.
mi _	immunomodulatory activity of	Additional preferred
lod	polypeptides of the invention	indications include idiopathic
(inc	(including antibodies and	pulmonary fibrosis. Highly
ago	agonists or antagonists of the	preferred indications include
vai	invention) include the assays	neoplastic diseases (e.g.,
disc	disclosed in Miraglia et al., J	leukemia, lymphoma,
Bio	Biomolecular Screening 4:193-	melanoma, and/or as described
 204	204 (1999); Rowland et al.,	below under
"Ly	"Lymphocytes: a practical	"Hyperproliferative
dde	approach" Chapter 6:138-160	Disorders"). Highly preferred
 (20)	(2000); Gonzalez et al., J Clin	indications include neoplasms
Lab	Lab Anal 8(5):225-233 (1995);	and cancers, such as, for
Bill	Billiau et al., Ann NY Acad	example, leukemia, lymphoma,
 Sci	Sci 856:22-32 (1998); Boehm	melanoma, and prostate,
eta	et al., Annu Rev Immunol	breast, lung, colon, pancreatic,
15:2	15:749-795 (1997), and	esophageal, stomach, brain,
Rhe	Rheumatology (Oxford)	liver and urinary cancer. Other
38(.	38(3):214-20 (1999), the	preferred indications include
con	contents of each of which are	benign dysproliferative
here	herein incorporated by	disorders and pre-neoplastic
refe	reference in its entirety.	conditions, such as, for
Hur	Human T cells that may be	example, hyperplasia,
 ) asc	used according to these assays	metaplasia, and/or dysplasia.
may may	may be isolated using	Preferred indications include
tech	techniques disclosed herein or	anemia, pancytopenia,
othe	otherwise known in the art.	leukopenia, thrombocytopenia,
 Hum	Human T cells are primary	Hodgkin's disease, acute
hum	human lymphocytes that	lymphocytic anemia (ALL).

below) and	immunodeficiencies (e.g., as	described below). Additional	highly preferred indications	include inflammation and	inflammatory disorders.	Highly preferred indications	also include neoplastic	diseases (e.g., leukemia,	lymphoma, and/or as described	below under	"Hyperproliferative	Disorders"). Highly preferred	indications include neoplasms	and cancers, such as, leukemia,	lymphoma, prostate, breast,	lung, colon, pancreatic,	esophageal, stomach, brain,	liver, and urinary cancer. Other	preferred indications include	benign dysproliferative	disorders and pre-neoplastic	conditions, such as, for	example, hyperplasia,	metaplasia, and/or dysplasia.	Preferred indications include	arthritis, asthma, AIDS,	allergy, anemia, pancytopenia,	leukopenia, thrombocytopenia,	Hodgkin"s disease, acute	lymphocytic anemia (ALL).
induced activity of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include the assays	disclosed in Forrer et al., Biol	Chem 379(8-9):1101-1110	(1998); Gupta et al., Exp Cell	Res 247(2): 495-504 (1999);	Kyriakis JM, Biochem Soc	Symp 64:29-48 (1999); Chang	and Karin, Nature	410(6824):37-40 (2001); and	Cobb MH, Prog Biophys Mol	Biol 71(3-4):479-500 (1999);	the contents of each of which	are herein incorporated by	reference in its entirety. T	cells that may be used	according to these assays are	publicly available (e.g.,	through the ATCC).	Exemplary mouse T cells that	may be used according to these	assays include the CTLL cell	line, which is an IL-2	dependent suspension-culture	cell line with cytotoxic	activity.		
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		•			plasmacytomas, multiple myeloma, Burkitt's lymphoma, granulomatous disease, inflammatory bowel disease, sepsis, psoriasis, suppression of immune reactions to transplanted organs and tissues, endocarditis,
99	HEEAG23	1113	Activation of Adipocyte ERK Signaling Pathway	Kinase assay. Kinase assays, for example an Elk-1 kinase assay, for ERK signal transduction that regulate cell proliferation or differentiation are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote or inhibit cell proliferation, activation, and differentiation. Exemplary assays for ERK kinase activity that may be used or routinely modified to test ERK kinase-induced activity of polypeptides of the invention (including antibodies and agonists or antagonists of	A highly preferred embodiment of the invention includes a method for stimulating adipocyte proliferation. An alternative highly preferred embodiment of the invention includes a method for inhibiting adipocyte proliferation. A highly preferred embodiment of the invention includes a method for stimulating adipocyte differentiation. An alternative highly preferred embodiment of the invention includes a method for inhibiting adipocyte differentiation. A highly preferred embodiment of the invention includes a method for inhibiting adipocyte differentiation. A highly preferred embodiment of the invention includes a method for stimulating (e.g.,
				the invention) include the	increasing) adipocyte

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assays disclosed in Forrer et al., Biol Chem 379(8-9):1101-1110 (1998); Le Marchand-Brustel Y, Exp Clin Endocrinol Diabetes 107(2):126-132 (1999); Kyriakis JM, Biochem Soc Symp 64:29-48 (1999); Chang and Karin, Nature 410(6824):37-40 (2001); and Cobb MH, Prog Biophys Mol Biol 71(3-4):479-500 (1999); the contents of each of which are herein incorporated by reference in its entirety. Mouse adipocyte cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary mouse adipocyte cells that may be used according to these assays include 3T3-L1 cells. 3T3-L1 is an adherent mouse preadipocyte cell line that is a continuous substrain of 3T3 fibroblast cells developed through clonal isolation and undergo a pre-adipocyte to adipose-like conversion under		activation. An alternative	highly preferred embodiment	of the invention includes a	method for inhibiting the	activation of (e.g., decreasing)	and/or inactivating adipocytes.	Highly preferred indications	include endocrine disorders	(e.g., as described below under	"Endocrine Disorders").	Highly preferred indications	also include neoplastic	diseases (e.g., lipomas,	liposarcomas, and/or as	described below under	"Hyperproliferative	Disorders"). Preferred	indications include blood	disorders (e.g., hypertension,	congestive heart failure, blood	vessel blockage, heart disease,	stroke, impotence and/or as	described below under	"Immune Activity",	"Cardiovascular Disorders",	and/or "Blood-Related	Disorders"), immune disorders	(e.g., as described below under	"Immune Activity"), neural	disorders (e.g., as described	
	1	assays disclosed in Forrer et	al., Biol Chem 379(8-9):1101-	1110 (1998); Le Marchand-	Brustel Y, Exp Clin	Endocrinol Diabetes	107(2):126-132 (1999);	Kyriakis JM, Biochem Soc	Symp 64:29-48 (1999); Chang	and Karin, Nature	410(6824):37-40 (2001); and	Cobb MH, Prog Biophys Mol	Biol 71(3-4):479-500 (1999);	the contents of each of which	are herein incorporated by	reference in its entirety.	Mouse adipocyte cells that	may be used according to these	assays are publicly available	(e.g., through the ATCC).	Exemplary mouse adipocyte	cells that may be used	according to these assays	include 3T3-L1 cells. 3T3-L1	is an adherent mouse	preadipocyte cell line that is a	continuous substrain of 3T3	fibroblast cells developed	through clonal isolation and	undergo a pre-adipocyte to	adipose-like conversion under	
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and Neurological Diseases"), and infection (e.g., as described below under "Infections Disease")	A highly preferred indication is diabetes mellitus. An additional highly preferred indication is a complication	associated with diabetes (e.g., diabetic retinopathy, diabetic nephropathy, kidney disease (e.g., renal failure.	nephropathy and/or other diseases and disorders as described in the "Renal Disorders" section below),	diabetic neuropathy, nerve disease and nerve damage (e.g., due to diabetic neuropathy), blood vessel blockage, heart disease, stroke,	impotence (e.g., due to diabetic neuropathy or blood vessel blockage), seizures, mental confusion, drowsiness,	nonketotic hyperglycemic- hyperosmolar coma, cardiovascular disease (e.g., heart disease, atherosclerosis, microvascular disease, hypertension, stroke, and other
conditions known in the art.						
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diseases and disorders as described in the "Cardiovascular Disorders" section below), dyslipidemia, endocrine disorders (as	described in the "Endocrine Disorders" section below), neuropathy, vision impairment (e.g., diabetic retinopathy and blindness), ulcers and impaired wound healing, infection (e.g., infections diseases and	disorders as described in the "Infectious Diseases" section below (particularly of the urinary tract and skin). An additional highly preferred indication is obesity and/or complications associated with obesity. Additional highly	preferred indications include weight loss or alternatively, weight gain. Additional highly preferred indications are complications associated with insulin resistance. Additional highly preferred indications are disorders of the musculoskeletal systems including myopathies, muscular dystrophy, and/or as

described herein.  Additional highly preferred indications include, hypertension, coronary artery disease, dyslipidemia, gallstones, osteoarthritis, degenerative arthritis, eating disorders. fibrosis, cachexia, and kidney diseases or disorders. Preferred indications include neoplasms and cancer, such as, lymphoma, leukemia and breast, colon, and kidney cancer. Additional preferred indications include melanoma, prostate, lung, pancreatic, esophageal, stomach, brain, liver, and urinary cancer. Highly preferred indications include lipomas and liposarcomas. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such	as, for example, hyperplasia, metaplasia, and/or dysplasia.		
		Glucose Production in H4IIE	CD69 in Human T cells
		1113	1113
		HEEAG23	HEEAG23
		165	165

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eq eq	inventi	for	sell surv	ıly prefe	inventi	for	cell	ferred	inventi	for	cell	specific	tal muse	stimula	ily prefe	inventi	for	ell	specific	tal muse	inhibit	liment o	des a	ting mu	In a	nt, skele	ntiation	ernative	nbodim	sludes a
preferi	it of the	nethod	nuscle (	ive high	it of the	nethod	muscle	A preferred	t of the	nethod	muscle	n. In a	it, skele	ation is	ive high	it of the	nethod	nuscle c	n. In a	it, skele	ation is	d emboo	on inclu	stimula	ntiation.	bodime	differe	An alte	erred en	ntion inc
A highly preferred	embodiment of the invention	includes a method for	increasing muscle cell survival	An alternative highly preferred	embodiment of the invention	includes a method for	decreasing muscle cell	survival.	embodiment of the invention	includes a method for	stimulating muscle cell	proliferation. In a specific	embodiment, skeletal muscle	cell proliferation is stimulated.	An alternative highly preferred	embodiment of the invention	includes a method for	inhibiting muscle cell	proliferation. In a specific	embodiment, skeletal muscle	cell proliferation is inhibited.	A preferred embodiment of	the invention includes a	method for stimulating muscle	cell differentiation. In a	specific embodiment, skeletal	muscle cell differentiation is	stimulated. An alternative	highly preferred embodiment	of the invention includes a
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assays,	kinase	ignal	ate	d cell	vn in th		ssess	des of	58	s or	ntion) t	ose	rvival.	213	y be	fied to	l activit		ntibodie	nists of	assays	I., Biol	110	:	_	tal.,	999	each of	porated	rety.
Zinase a	GSK-3	inase s	ıt regula	lism an	ll-knov	used or	ied to a	lypepti	ncludin	agonist	he inve	bit gluc	l cell su	ys for.I	hat ma	y modi	induced	of the	ıding ar	antago	nclude	rrer et a	:1101-1	na et al	263-27	reyer e	1662-1	tents of	n incor	its enti
ıssay.	ıple an	or PI3 l	tion tha	metabo	l are we	nay be	y modif	ty of pc	ntion (i	es and	ists of t	or inhi	ism and	ary assa	ctivity 1	routinel	kinase-	eptides	n (inclu	nists or	ntion) i	d in Fo	(6-8)62	Nikouli	s 49(2):	and Sch	s 48(8):	the con	re herei	ence in
Kinase assay. Kinase assays,	for example an GSK-3 kinase	assay, for PI3 kinase signal	transduction that regulate	glucose metabolism and cell	survivial are well-known in the	art and may be used or	routinely modified to assess	the ability of polypeptides of	the invention (including	antibodies and agonists or	antagonists of the invention) to	promote or inhibit glucose	metabolism and cell survival.	Exemplary assays for PI3	kinase activity that may be	used or routinely modified to	test PI3 kinase-induced activity	of polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) include assays	disclosed in Forrer et al., Biol	Chem 379(8-9):1101-1110	(1998); Nikoulina et al.,	Diabetes 49(2):263-271	(2000); and Schreyer et al.,	Diabetes 48(8):1662-1666	(1999), the contents of each of	which are herein incorporated	by reference in its entirety.
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ou of	Mucle	ase	ng Path																											
Activation of	Skeletal Mucle Cell	PI3 Kinase	Signalling Pathway																											
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	165																													

method for inhibiting muscle cell differentiation. In a specific embodiment, skeletal muscle cell differentiation is inhibited. Highly preferred	indications include disorders of the musculoskeletal system. Preferred indications include	neoplastic diseases (e.g., as described below under "Hyperproliferative"	Disorders"), endocrine disorders (e.g., as described	below under "Endocrine Disorders"), neural disorders	(e.g., as described below under "Neural Activity and	Neurological Diseases"), blood	disorders (e.g., as described below under "Immune	Activity", "Cardiovascular Disorders", and/or "Blood-	Related Disorders"), immune	disorders (e.g., as described below under "Immune	Activity"), and infection (e.g.,	as described below under	ation	diabetes mellitus. An
Rat myoblast cells that may be used according to these assays are publicly available (e.g., through the ATCC).  Exemplary rat myoblast cells	that may be used according to these assays include L6 cells. L6 is an adherent rat myoblast	cell line, isolated from primary cultures of rat thigh muscle, that fuses to form	multinucleated myotubes and striated fibers after culture in	differentiation media.										
		P) - P)												

indication is a complication	associated with diabetes (e.g.,	diabetic retinopathy, diabetic	nephropathy, kidney disease	(e.g., renal failure,	nephropathy and/or other	diseases and disorders as	described in the "Renal	Disorders" section below),	diabetic neuropathy, nerve	disease and nerve damage (e.g.,	due to diabetic neuropathy),	blood vessel blockage, heart	disease, stroke, impotence	(e.g., due to diabetic	neuropathy or blood vessel	blockage), seizures, mental	confusion, drowsiness,	nonketotic hyperglycemic-	hyperosmolar coma,	cardiovascular disease (e.g.,	heart disease, atherosclerosis,	microvascular disease,	hypertension, stroke, and other	diseases and disorders as	described in the	"Cardiovascular Disorders"	section below), dyslipidemia,	endocrine disorders (as	described in the "Endocrine	Disorders" section below).
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neuropathy, vision impairment	(e.g., diabetic retinopathy and	blindness), ulcers and impaired	wound healing, infections	(e.g., infectious diseases and	disorders as described in the	"Infectious Diseases" section	below, especially of the	urinary tract and skin), carpal	tunnel syndrome and	Dupuytren's contracture).	An additional highly preferred	indication is obesity and/or	complications associated with	obesity. Additional highly	preferred indications include	weight loss or alternatively,	weight gain. Additional	highly preferred indications are	complications associated with	insulin resistance.	Additonal highly preferred	indications are disorders of the	musculoskeletal system	including myopathies,	muscular dystrophy, and/or as	described herein.	Additional highly preferred	indications include: myopathy,	atrophy, congestive heart	failure, cachexia, myxomas,

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fibromas, congenital cardiovascular abnormalities, heart disease, cardiac arrest, heart valve disease, and vascular disease. Highly preferred indications include neoplasms and cancer, such as, rhabdomyoma, rhabdosarcoma, stomach, esophageal, prostate, and urinary cancer. Preferred indications also include breast, lung, colon, pancreatic, brain, and liver cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, hyperplasia, metaplasia, and/or dysplasia.			Preferred indications include neoplastic diseases (e.g., as described below under "Hyperproliferative"	Disorders"), blood disorders (e.g., as described below under "Immune Activity",
			Assays for the activation of transcription through the AP1 response element are known in the art and may be used or	routinely modified to assess the ability of polypeptides of the invention (including
	SEAP in OE-33	SEAP in 3T3L1	Activation of transcription through AP1 response element in	immune cells (such as T-cells).
	1113	1114	1114	
	HEEAG23	HEEAJ02	HEEAJ02	
	165	166	166	

	antibodies and agonists or	"Cardiovascular Disorders",
	antagonists of the invention) to	and/or "Blood-Related
	modulate growth and other cell	Disorders"), and infection
	functions. Exemplary assays	(e.g., an infectious disease as
-	for transcription through the	described below under
	AP1 response element that	"Infectious Disease"). Highly
	may be used or routinely	preferred indications include
	modified to test AP1-response	autoimmune diseases (e.g.,
	element activity of	rheumatoid arthritis, systemic
	polypeptides of the invention	lupus erythematosis, multiple
	(including antibodies and	sclerosis and/or as described
	agonists or antagonists of the	below) and
	invention) include assays	immunodeficiencies (e.g., as
	disclosed in Berger et al., Gene	described below). Additional
	66:1-10 (1988); Cullen and	highly preferred indications
	Malm, Methods in Enzymol	include inflammation and
	216:362-368 (1992); Henthorn	inflammatory disorders.
	et al., Proc Natl Acad Sci USA	Highly preferred indications
	85:6342-6346 (1988);	also include neoplastic
	Rellahan et al., J Biol Chem	diseases (e.g., leukemia,
	272(49):30806-30811 (1997);	lymphoma, and/or as described
	Chang et al., Mol Cell Biol	below under
	18(9):4986-4993 (1998); and	"Hyperproliferative
	Fraser et al., Eur J Immunol	Disorders"). Highly preferred
	29(3):838-844 (1999), the	indications include neoplasms
	contents of each of which are	and cancers, such as, leukemia,
	herein incorporated by	lymphoma, prostate, breast,
	reference in its entirety. T	lung, colon, pancreatic,
	cells that may be used	esophageal, stomach, brain,
	according to these assays are	liver, and urinary cancer. Other
	publicly available (e.g.,	preferred indications include

display the call and the control of	of A preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) TNF alpha production. An alternative preferred embodiment of the invention includes a method for stimulating (e.g., increasing) TNF alpha on) to production. Preferred indications include blood
through the ATCC).  Exemplary mouse T cells that may be used according to these assays include the CTLL cell line, which is an IL-2 dependent suspension-culture cell line with cytotoxic activity.	Assays for the activation of transcription through the Serum Response Element (SRE) are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate the serum response
	Activation of transcription through serum response element in immune cells (such as T-cells).
	1114
	HEEAJ02
	166

factors and modulate the	ate the	disorders (e.g., as described
expression of genes involved	es involved	below under "Immune
in growth. Exemplary assays	olary assays	Activity", "Blood-Related
for transcription through the	hrough the	Disorders", and/or
SRE that may be used or	used or	"Cardiovascular Disorders"),
routinely modified to test SRE	d to test SRE	Highly preferred indications
activity of the polypeptides of	ypeptides of	include autoimmune diseases
the invention (including	luding	(e.g., rheumatoid arthritis,
antibodies and agonists or	onists or	systemic lupus erythematosis,
antagonists of the invention)	invention)	Crohn"s disease, multiple
include assays disclosed in	closed in	sclerosis and/or as described
Berger et al., Gene 66:1-10	e 66:1-10	below), immunodeficiencies
(1998); Cullen and Malm,	d Malm,	(e.g., as described below),
Methods in Enzymol 216:362-	nol 216:362-	boosting a T cell-mediated
368 (1992); Henthorn et al.,	norn et al.,	immune response, and
Proc Natl Acad Sci USA	si USA	suppressing a T cell-mediated
85:6342-6346 (1988); and	88); and	immune response. Additional
Black et al., Virus Genes	Genes	highly preferred indications
12(2):105-117 (1997), the	97), the	include inflammation and
content of each of which are	which are	inflammatory disorders, and
herein incorporated by	d by	treating joint damage in
reference in its entirety.	tirety. T	patients with rheumatoid
cells that may be used	pesr	arthritis. An additional highly
according to these assays are	assays are	preferred indication is sepsis.
publicly available (e.g.,	(e.g.,	Highly preferred indications
through the ATCC).		include neoplastic diseases
Exemplary mouse T cells that	T cells that	(e.g., leukemia, lymphoma,
may be used according to these	rding to these	and/or as described below
assays include the CTLL cell	CTLL cell	under "Hyperproliferative
line, which is an IL-2	L-2	Disorders"). Additionally,
dependent suspension culture	sion culture	highly preferred indications

		of T cells with cytotoxic	include neoplasms and
		activity.	leukemia, lymphoma,
	J.		melanoma, glioma (e.g.,
			malignant glioma), solid
			tumors, and prostate, breast,
	****		lung, colon, pancreatic,
			esophageal, stomach, brain,
			liver and urinary cancer. Other
			preferred indications include
			benign dysproliferative
			disorders and pre-neoplastic
			conditions, such as, for
			example, hyperplasia,
			metaplasia, and/or dysplasia.
			Preferred indications include
			anemia, pancytopenia,
			leukopenia, thrombocytopenia,
			Hodgkin's disease, acute
			lymphocytic anemia (ALL),
			plasmacytomas, multiple
nd a mark d			myeloma, Burkitt's lymphoma,
			arthritis, AIDS, granulomatous
			disease, inflammatory bowel
			disease, neutropenia,
			neutrophilia, psoriasis,
			suppression of immune
			reactions to transplanted
			organs and tissues,
			hemophilia, hypercoagulation,
			diabetes mellitus, endocarditis,

meningitis, Lyme Disease, cardiac reperfusion injury, and asthma and allergy. An additional preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease").	
	Assays for the regulation (i.e. increases or decreases) of viability and proliferation of cells in vitro are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate viability and proliferation of pre-adipose cells and cell lines. For example, the CellTiter-Gloô Luminescent Cell Viability Assay (Promega Corp., Madison, WI, USA) can be used to measure the number of viable cells in culture based on quantitation of the ATP presence of metabolically active cells. 3T3-L1 is a mouse preadipocyte cell line. It
	Proliferation of preadipose cells (such as 3T3-L1 cells)
	1114
	HEEAJ02
	166

		Highly preferred indications include eosinophilia, asthma, allergy, hypersensitivity reactions, inflammation, and inflammatory disorders.  Additional highly preferred indications include immune and hematopoietic disorders (e.g., as described below under "Immune Activity", and "Blood-Related Disorders"), autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, Crohn"s disease, multiple sclerosis and/or as described below), immunodeficiencies (e.g., as described below), Highly
is a continuous substrain of 3T3 fibroblast cells developed through clonal isolation. Cells were differentiated to an adipose-like state before being used in the screen. See Green H and Meuth M., Cell 3: 127-133 (1974), which is herein incorporated by reference in its entirety.		Assays for the regulation (i.e. increases or decreases) of viability and proliferation of cells in vitro are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate viability and proliferation of eosinophil cells and cell lines. For example, the CellTiter-Gloô  Luminescent Cell Viability Assay (Promega Corp., Madison, WI, USA) can be used to measure the number of
	SEAP in Jurkat/IL4 promoter (antiCD3 co-stim)	Regulation of viability or proliferation of immune cells (such as human eosinophil EOL-1 cells).
	1114	1115
	HEEAJ02	HEEAQ11
	166	167

		2		viable cells in culture based on	preferred indications also
				quantitation of the ATF present which signals the	immune cell proliferation.
				presence of metabolically	Preferred indications include
				active cells. Eosinophils are a	neoplastic diseases (e.g.,
			,	type of immune cell important	leukemia, lymphoma, and/or as
-				in allergic responses; they are	described below under
145				recruited to tissues and	"Hyperproliferative
				mediate the inflammtory	Disorders"). Highly preferred
				response of late stage allergic	indications include boosting an
		····		reaction. Eosinophil cell lines	eosinophil-mediated immune
				that may be used according to	response, and suppressing an
				these assays are publicly	eosinophil-mediated immune
				available and/or may be	response.
				routinely generated.	
				Exemplary eosinophil cells	
				that may be used according to	
				these assays include EOL-1	
				Cells.	
	HEEAQ11	1115	Activation of T-	Kinase assay. JNK and p38	Preferred indications include
167			Cell p38 or JNK	kinase assays for signal	neoplastic diseases (e.g., as
			Signaling Pathway.	transduction that regulate cell	described below under
				proliferation, activation, or	"Hyperproliferative
				apoptosis are well known in	Disorders"), blood disorders
				the art and may be used or	(e.g., as described below under
				routinely modified to assess	"Immune Activity",
				the ability of polypeptides of	"Cardiovascular Disorders",
				the invention (including	and/or "Blood-Related
-				antibodies and agonists or	Disorders"), and infection
			-	antagonists of the invention) to	(e.g., an infectious disease as
				promote or inhibit immune cell	described below under

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activation, and apoptosis.	preferred indications include
Exemplary assays for JNK and	autoimmune diseases (e.g.,
p38 kinase activity that may be	rheumatoid arthritis, systemic
used or routinely modified to	lupus erythematosis, multiple
test JNK and p38 kinase-	sclerosis and/or as described
induced activity of	below) and
polypeptides of the invention	immunodeficiencies (e.g., as
(including antibodies and	described below). Additional
agonists or antagonists of the	highly preferred indications
invention) include the assays	include inflammation and
disclosed in Forrer et al., Biol	inflammatory disorders.
Chem 379(8-9):1101-1110	Highly preferred indications
(1998); Gupta et al., Exp Cell	also include neoplastic
Res 247(2): 495-504 (1999);	diseases (e.g., leukemia,
Kyriakis JM, Biochem Soc	lymphoma, and/or as described
Symp 64:29-48 (1999); Chang	below under
and Karin, Nature	"Hyperproliferative
410(6824):37-40 (2001); and	Disorders"). Highly preferred
Cobb MH, Prog Biophys Mol	indications include neoplasms
Biol 71(3-4):479-500 (1999);	and cancers, such as, leukemia,
the contents of each of which	lymphoma, prostate, breast,
are herein incorporated by	lung, colon, pancreatic,
reference in its entirety. T	esophageal, stomach, brain,
cells that may be used	liver, and urinary cancer. Other
according to these assays are	preferred indications include
publicly available (e.g.,	benign dysproliferative
through the ATCC).	disorders and pre-neoplastic
Exemplary mouse T cells that	conditions, such as, for
may be used according to these	example, hyperplasia,
assays include the CTLL cell	metaplasia, and/or dysplasia.
	activation, and apoptosis. Exemplary assays for JNK and p38 kinase activity that may be used or routinely modified to test JNK and p38 kinase-induced activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include the assays disclosed in Forrer et al., Biol Chem 379(8-9):1101-1110 (1998); Gupta et al., Exp Cell Res 247(2): 495-504 (1999); Kyriakis JM, Biochem Soc Symp 64:29-48 (1999); Chang and Karin, Nature 410(6824):37-40 (2001); and Cobb MH, Prog Biophys Mol Biol 71(3-4):479-500 (1999); the contents of each of which are herein incorporated by reference in its entirety. T cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary mouse T cells that may be used according to these assays include the CTLL cell

				line, which is an IL-2 dependent suspension-culture cell line with cytotoxic activity.	Preferred indications include arthritis, asthma, AIDS, allergy, anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin"s disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt"s lymphoma, granulomatous disease, inflammatory bowel disease, sepsis, psoriasis, suppression of immune reactions to transplanted organs and tissues, endocarditis,
191	HEEAQ11	1115	CD71 in Human T cells		membros, and plus process.
168	HEEBI05	1116	Activation of transcription through NFAT response element in immune cells (such as mast cells).	This reporter assay measures activation of the NFAT signaling pathway in HMC-1 human mast cell line. Activation of NFAT in mast cells has been linked to cytokine and chemokine production. Assays for the activation of transcription through the Nuclear Factor of Activated T cells (NFAT) response element are well-known in the art and may be used or routinely modified to	Highly preferred indications include allergy, asthma, and rhinitis. Additional preferred indications include infection (e.g., an infectious disease as described below under "Infectious Disease"), and inflammatory disorders. Preferred indications also include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or

	assess the ability of	"Cardiovascular Disorders")
	polypeptides of the invention	Preferred indications include
	(including antibodies and	autoimmune diseases (e.g.,
	agonists or antagonists of the	rheumatoid arthritis, systemic
	invention) to regulate NFAT	lupus erythematosis, multiple
<del></del>	transcription factors and	sclerosis and/or as described
<u> </u>	modulate expression of genes	below) and
•	involved in	immunodeficiencies (e.g., as
-	immunomodulatory functions.	described below). Preferred
	Exemplary assays for	indications include neoplastic
· ·	transcription through the	diseases (e.g., leukemia,
	NFAT response element that	lymphoma, melanoma,
<u></u>	may be used or routinely	prostate, breast, lung, colon,
=	modified to test NFAT-	pancreatic, esophageal,
-	response element activity of	stomach, brain, liver, and
	polypeptides of the invention	urinary tract cancers and/or as
	(including antibodies and	described below under
	agonists or antagonists of the	"Hyperproliferative
·==	invention) include assays	Disorders"). Other preferred
0	disclosed in Berger et al., Gene	indications include benign
9	66:1-10 (1998); Cullen and	dysproliferative disorders and
	Malm, Methods in Enzymol	pre-neoplastic conditions, such
	216:362-368 (1992); Henthorn	as, for example, hyperplasia,
9	et al., Proc Natl Acad Sci USA	metaplasia, and/or dysplasia.
	85:6342-6346 (1988); De Boer	Preferred indications include
<u>•</u>	et al., Int J Biochem Cell Biol	anemia, pancytopenia,
	31(10):1221-1236 (1999); Ali	leukopenia, thrombocytopenia,
<u>a)</u>	et al., J Immunol	leukemias, Hodgkin's disease,
	165(12):7215-7223 (2000);	acute lymphocytic anemia
1	Hutchinson and McCloskey, J	(ALL), plasmacytomas,
	Biol Chem 270(27):16333-	multiple myeloma, Burkitt's

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lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, and Lyme Disease.	A highly preferred embodiment of the invention includes a method for stimulating endothelial cell growth. An alternative highly preferred embodiment of the invention includes a method for inhibiting endothelial cell growth. A highly preferred embodiment of the invention includes a method for stimulating endothelial cell stimulating endothelial cell
16338 (1995), and Turner et al., J Exp Med 188:527-537 (1998), the contents of each of which are herein incorporated by reference in its entirety.  Mast cells that may be used according to these assays are publicly available (e.g., through the ATCC).  Exemplary human mast cells that may be used according to include the HMC-1 cell line, which is an immature human mast cell line established from the peripheral blood of a patient with mast cell leukemia, and exhibits many characteristics of immature mast cells.	Caspase Apoptosis. Assays for caspase apoptosis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote caspase protease-mediated apoptosis. Induction of apoptosis in endothelial cells supporting the
	Apoptosis
	1117
	HEGAH43
	169

		vasculature of tumore is	proliferation An alternative	_
		vascaidiuis of tuillois is	proniciation. An ancinative	
		associated with tumor	highly preferred embodiment	
		regression due to loss of tumor	of the invention includes a	
		blood supply. Exemplary	method for inhibiting	
		assays for caspase apoptosis	endothelial cell proliferation.	
		that may be used or routinely	A highly preferred	
		modified to test capase	embodiment of the invention	
		apoptosis activity of	includes a method for	
		polypeptides of the invention	stimulating apoptosis of	
		(including antibodies and	endothelial cells. An	
		agonists or antagonists of the	alternative highly preferred	
-		invention) include the assays	embodiment of the invention	
		disclosed in Lee et al., FEBS	includes a method for	
18/48		Lett 485(2-3): 122-126 (2000);	inhibiting (e.g., decreasing)	
		Nor et al., J Vasc Res 37(3):	apoptosis of endothelial cells.	
		209-218 (2000); and Karsan	A highly preferred	
		and Harlan, J Atheroscler	embodiment of the invention	
		Thromb 3(2): 75-80 (1996);	includes a method for	
		the contents of each of which	stimulating angiogenisis. An	
		are herein incorporated by	alternative highly preferred	
		reference in its entirety.	embodiment of the invention	
		Endothelial cells that may be	includes a method for	
	_	used according to these assays	inhibiting angiogenesis. A	
		are publicly available (e.g.,	highly preferred embodiment	
		through commercial sources).	of the invention includes a	
		Exemplary endothelial cells	method for reducing cardiac	
	_	that may be used according to	hypertrophy. An alternative	
		these assays include bovine	highly preferred embodiment	
		aortic endothelial cells	of the invention includes a	
		(bAEC), which are an example	method for inducing cardiac	
	_	of endothelial cells which line	hypertrophy Highly	

		heart failure, hypertension, aortic stenosis, cardiomyopathy, valvular regurgitation, left ventricular	dysfunction, atherosclerosis and atherosclerotic vascular	disease, diabetic nephropathy, intracardiac shunt, cardiac	hypertrophy, myocardial infarction, chronic	hemodynamic overload, and/or as described below under	"Cardiovascular Disorders"). Highly preferred indications	include cardiovascular, endothelial and/or angiogenic	disorders (e.g., systemic	such as diabetes mellitus, as	well as diseases of the vessels themselves, such as of the	arteries, capillaries, veins and/or lymphatics). Highly	preferred are indications that
blood vessels and are involved in functions that include, but are not limited to,	permeability, vascular tone, and immune cell extravasation.												
				1 1					•				

stimulate angiogenesis and/or cardiovascularization. Highly preferred are indications that inhibit angiogenesis and/or	Cardiovascularization.  Highly preferred indications include antiangiogenic activity to treat solid tumors,	sarcoma, and retinal disorders. Highly preferred indications include neoplasms and cancer, such as, Kaposi"s sarcoma.	hemangioma (capillary and cavernous), glomus tumors, telangiectasia, bacillary	angiomatosis, hemangioendothelioma, angiosarcoma, haemangiopericytoma, lymphangioma, lymphangiosarcoma. Highly preferred indications also include cancers such as,	prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver, and urinary cancer. Preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such
					-

as, for example, hyperplasia, metaplasia, and/or dysplasia. Highly preferred indications also include arterial disease,	such as, atherosclerosis, hypertension, coronary artery disease, inflammatory vasculitides, Reynaud"s disease and Reynaud"s phenomenom, aneurysms,	restenosis; venous and lymphatic disorders such as thrombophlebitis, lymphangitis, and lymphedema; and other vascular disorders such as	peripheral vascular disease, and cancer. Highly preferred indications also include trauma such as wounds, burns, and injured tissue (e.g., vascular injury such as. injury resulting from	balloon angioplasty, and atheroschlerotic lesions), implant fixation, scarring, ischemia reperfusion injury, rheumatoid arthritis, cerebrovascular disease, renal diseases such as acute renal failure, and osteonorosis

Additional highly preferred	indications include stroke,	graft rejection, diabetic or	other retinopathies, thrombotic	and coagulative disorders,	vascularitis, lymph	angiogenesis, sexual disorders,	age-related macular	degeneration, and treatment	/prevention of endometriosis	and related conditions.	Additional highly preferred	indications include fibromas,	heart disease, cardiac arrest,	heart valve disease, and	vascular disease.	Preferred indications include	blood disorders (e.g., as	described below under	"Immune Activity", "Blood-	Related Disorders", and/or	"Cardiovascular Disorders").	Preferred indications include	autoimmune diseases (e.g.,	rheumatoid arthritis, systemic	lupus erythematosis, multiple	sclerosis and/or as described	below) and	immunodeficiencies (e.g., as	described below). Additional	preferred indications include
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											<u> </u>								,											
					•																							•		

inflammation and inflammatory disorders (such as acute and chronic inflammatory diseases, e.g., inflammatory bowel disease and Crohn's disease), and pain management.		>	of the Inflammation, Vascular CAM-1 Disease, Athereosclerosis, assays Restenosis, and Stroke	AM-1 ays et al, 81 o K, et nts of	nce in its y be
		expression of ICAM-1 are well-known in the art and may be used or routinely modified to assess the ability of polymentides of the invention	(including antibodies and agonists or antagonists of the invention) to regulate ICAM-1 expression. Exemplary assays that may be used or routinely	modified to measure ICAM-1 expression include assays disclosed in: Takacs P, et al, FASEB J, 15(2):279-281 (2001); and, Miyamoto K, et al., Am J Pathol, 156(5):1733-1739 (2000), the contents of	each of which is herein incorporated by reference in its entirety. Cells that may be
	SEAP in HIB/CRE	ICAM-1			- Tables
	1117				
	HEGAH43				
`	169	170			

				are publicly available (e.g., through the ATCC) and/or	
				may be routinely generated.	
				Exemplary cells that may be	
				used according to these assays	
				include microvascular	
	7011			endothelial cells (MVEC).	
170	HEGAN94	1118	ICAM in OE19		
,	HEGBS69	1119	Production of IL-6	IL-6 FMAT. IL-6 is produced	A highly preferred
171	-			by T cells and has strong	embodiment of the invention
				effects on B cells. IL-6	includes a method for
				participates in IL-4 induced	stimulating (e.g., increasing)
				IgE production and increases	IL-6 production. An alternative
				IgA production (IgA plays a	highly preferred embodiment
				role in mucosal immunity).	of the invention includes a
		15-11-		IL-6 induces cytotoxic T cells.	method for inhibiting (e.g.,
				Deregulated expression of IL-6	reducing) IL-6 production. A
				has been linked to autoimmune	highly preferrred indication is
				disease, plasmacytomas,	the stimulation or enhancement
				myelomas, and chronic	of mucosal immunity. Highly
	-			hyperproliferative diseases.	preferred indications include
			-	Assays for immunomodulatory	blood disorders (e.g., as
	-			and differentiation factor	described below under
			-	proteins produced by a large	"Immune Activity", "Blood-
				variety of cells where the	Related Disorders", and/or
				expression level is strongly	"Cardiovascular Disorders"),
	-			regulated by cytokines, growth	and infection (e.g., as
				factors, and hormones are well	described below under
				known in the art and may be	"Infectious Disease"). Highly
				used or routinely modified to	preferred indications include

1992	assess the ability of	autoimmune diseases (e.g.
 	polypentides of the invention	rhenmatoid arthritis systemic
	(including antibodies and	lupus erythematosis, multiple
	agonists or antagonists of the	sclerosis and/or as described
PARALI	invention) to mediate	below) and
	immunomodulation and	immunodeficiencies (e.g., as
	differentiation and modulate T	described below). Highly
	cell proliferation and function.	preferred indications also
 	Exemplary assays that test for	include boosting a B cell-
	immunomodulatory proteins	mediated immune response
	evaluate the production of	and alternatively suppressing a
	cytokines, such as IL-6, and	B cell-mediated immune
	the stimulation and	response. Highly preferred
	upregulation of T cell	indications include
	proliferation and functional	inflammation and
	activities. Such assays that	inflammatory
	may be used or routinely	disorders.Additional highly
	modified to test	preferred indications include
	immunomodulatory and	asthma and allergy. Highly
	diffferentiation activity of	preferred indications include
	polypeptides of the invention	neoplastic diseases (e.g.,
	(including antibodies and	myeloma, plasmacytoma,
	agonists or antagonists of the	leukemia, lymphoma,
•	invention) include assays	melanoma, and/or as described
	disclosed in Miraglia et al., J	below under
	Biomolecular Screening 4:193-	"Hyperproliferative
	204(1999); Rowland et al.,	Disorders"). Highly preferred
	"Lymphocytes: a practical	indications include neoplasms
	approach" Chapter 6:138-160	and cancers, such as, myeloma,
	(2000); and Verhasselt et al., J	plasmacytoma, leukemia,
	Immunol 158: 2919-2925	lymphoma, melanoma, and

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prostate, breast, lung, colon.	pancreatic, esophageal,	stomach, brain, liver and	urinary cancer. Other preferred	indications include benign	dysproliferative disorders and	pre-neoplastic conditions, such	as, for example, hyperplasia,	metaplasia, and/or dysplasia.	Preferred indications include	anemia, pancytopenia,	leukopenia, thrombocytopenia,	Hodgkin's disease, acute	lymphocytic anemia (ALL),	multiple myeloma, Burkitt's	lymphoma, arthritis, AIDS,	granulomatous disease,	inflammatory bowel disease,	sepsis, neutropenia,	neutrophilia, psoriasis,	suppression of immune	reactions to transplanted	organs and tissues,	hemophilia, hypercoagulation,	diabetes mellitus, endocarditis,	meningitis, and Lyme Disease.	An additonal preferred	indication is infection (e.g., an	infectious disease as described	below under "Infectious	Disease")
(1997), the contents of each of	which are herein incorporated	by reference in its entirety.	Human dendritic cells that may	be used according to these	assays may be isolated using	techniques disclosed herein or	otherwise known in the art.	Human dendritic cells are	antigen presenting cells in	suspension culture, which,	when activated by antigen	and/or cytokines, initiate and	upregulate T cell proliferation	and functional activities.														4,000		
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																		tion				. 100								
									-	•																				

171	HEGBS69	1119	CD152 in Human T cells		
,	HELGK31	1120	Production of IL-6	IL-6 FMAT. IL-6 is produced	A highly preferred
172	•			by T cells and has strong	embodiment of the invention
				effects on B cells. IL-6	includes a method for
				participates in IL-4 induced	stimulating (e.g., increasing)
				IgE production and increases	IL-6 production. An alternative
				IgA production (IgA plays a	highly preferred embodiment
				role in mucosal immunity).	of the invention includes a
				IL-6 induces cytotoxic T cells.	method for inhibiting (e.g.,
				Deregulated expression of IL-6	reducing) IL-6 production. A
				has been linked to autoimmune	highly preferrred indication is
		···		disease, plasmacytomas,	the stimulation or enhancement
				myelomas, and chronic	of mucosal immunity. Highly
				hyperproliferative diseases.	preferred indications include
27				Assays for immunomodulatory	blood disorders (e.g., as
				and differentiation factor	described below under
				proteins produced by a large	"Immune Activity", "Blood-
				variety of cells where the	Related Disorders", and/or
		-		expression level is strongly	"Cardiovascular Disorders"),
				regulated by cytokines, growth	and infection (e.g., as
	<del></del>			factors, and hormones are well	described below under
				known in the art and may be	"Infectious Disease"). Highly
				used or routinely modified to	preferred indications include
_				assess the ability of	autoimmune diseases (e.g.,
				polypeptides of the invention	rheumatoid arthritis, systemic
				(including antibodies and	lupus erythematosis, multiple
				agonists or antagonists of the	sclerosis and/or as described
				invention) to mediate	below) and
				immunomodulation and	immunodeficiencies (e.g., as
				differentiation and modulate T	described below). Highly

Exemplary assays that test for include boosting a B cellmentation of cytokines, such as IL-6, and the stimulation and through assays that the stimulation and cytokines, such as IL-6, and the stimulation and through a cytokines, such as IL-6, and the stimulation and through a cytokines, such as IL-6, and the stimulation and cytokines, such as IL-6, and the stimulation and alternatively suppregulation of T cell inflammation and activities. Such assays that may be used or routinely may be used or routinely modified to test immunomodulatory and differentiation activity of modified to test immunomodulatory and alternation activity of preferred indications include polypeptides of the invention include assays invention) include assays invention) include assays invention) include assays invention include assays include inflammation and cancers, such as include inflammation include assays include	3. J.
Exemplary assays that test for immunomodulatory proteins evaluate the production of cytokines, such as IL-6, and the stimulation and upregulation of T cell proliferation and functional activities. Such assays that may be used or routinely modified to test immunomodulatory and diffferentiation activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Miraglia et al., J Biomolecular Screening 4:193-204(1999); Rowland et al., "Lymphocytes: a practical approach" Chapter 6:138-160 (2000); and Verhasselt et al., J Immunol 158:2919-2925 (1997), the contents of each of which are herein incorporated by reference in its entirety. Human dendritic cells that may be used according to these	Exemplary assays that test for immunomodulatory proteins evaluate the production of cytokines, such as IL-6, and the stimulation and upregulation of T cell proliferation and functional activities. Such assays that may be used or routinely modified to test immunomodulatory and differentiation activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Miraglia et al., J. Biomolecular Screening 4:193-204(1999); Rowland et al., "Lymphocytes: a practical approach" Chapter 6:138-160 (2000); and Verhasselt et al., J. Immunol 158:2919-2925 (1997), the contents of each of which are herein incorporated by reference in its entirety. Human dendritic cells that may be used according to these assays may be isolated using

as, for example, hyperplasia, art.  metaplasia, and/or dysplasia.  Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, and Lyme Disease.  An additonal preferred indication is infectious described below under "Infectious Disease").	A highly preferred  mune embodiment of the invention  ed to be includes a method for  skine. stimulating the production of  IFNg. An alternative highly  preferred embodiment of the  invention includes a method
otherwise known in the art.  Human dendritic cells are antigen presenting cells in suspension culture, which, when activated by antigen and/or cytokines, initiate and upregulate T cell proliferation and functional activities.	IFNgamma FMAT. IFNg plays a central role in the immune system and is considered to be a proinflammatory cytokine.  IFNg promotes TH1 and inhibits TH2 differentiation; promotes IgG2a and inhibits
	1120 Production of IFNgamma using a T cells
	HELGK31
	172

	IgE secretion; induces macrophage activation; and	for inhibiting the production of IFNg. Highly preferred
	increases MHC expression.	ions
	Assays for immunomodulatory	disorders (e.g., as described
	proteins produced by T cells	below under "Immune
	and NK cells that regulate a	Activity", "Blood-Related
	variety of inflammatory	Disorders", and/or
	activities and inhibit TH2	"Cardiovascular Disorders"),
	helper cell functions are well	and infection (e.g., viral
	known in the art and may be	infections, tuberculosis,
	used or routinely modified to	infections associated with
-	assess the ability of	chronic granulomatosus
	polypeptides of the invention	disease and malignant
	(including antibodies and	osteoporosis, and/or as
	agonists or antagonists of the	described below under
	invention) to mediate	"Infectious Disease"). Highly
	immunomodulation, regulate	preferred indications include
	inflammatory activities,	autoimmune disease (e.g.,
	modulate TH2 helper cell	rheumatoid arthritis, systemic
	function, and/or mediate	lupus erythematosis, multiple
	humoral or cell-mediated	sclerosis and/or as described
-	immunity. Exemplary assays	below), immunodeficiency
	that test for	(e.g., as described below),
	immunomodulatory proteins	boosting a T cell-mediated
	evaluate the production of	immune response, and
	cytokines, such as Interferon	suppressing a T cell-mediated
	gamma (IFNg), and the	immune response. Additional
	activation of T cells. Such	highly preferred indications
	assays that may be used or	include inflammation and
	routinely modified to test	inflammatory disorders.
	immunomodulatory activity of	Additional preferred

polypep	polypeptides of the invention (including antibodies and	indications include idiopathic
agonists	agonists or antagonists of the	
inventio	invention) include the assays	neoplastic diseases (e.g.,
disclose	disclosed in Miraglia et al., J	leukemia, lymphoma,
Biomole	93-	melanoma, and/or as described
204 (19	204 (1999); Rowland et al.,	below under
Trymph	"Lymphocytes: a practical	"Hyperproliferative
approac	approach" Chapter 6:138-160	Disorders"). Highly preferred
(2000);	(2000); Gonzalez et al., J Clin	indications include neoplasms
Lab Ana	Lab Anal 8(5):225-233 (1995);	and cancers, such as, for
Billian e Billian e	Billiau et al., Ann NY Acad	example, leukemia, lymphoma,
Sci 856	Sci 856:22-32 (1998); Boehm	melanoma, and prostate,
et al., A	et al., Annu Rev Immunol	breast, lung, colon, pancreatic,
15:749-	15:749-795 (1997), and	esophageal, stomach, brain,
Rheuma	Rheumatology (Oxford)	liver and urinary cancer. Other
38(3):21	38(3):214-20 (1999), the	preferred indications include
contents	contents of each of which are	benign dysproliferative
herein ii	herein incorporated by	disorders and pre-neoplastic
reference	reference in its entirety.	conditions, such as, for
Human	Human T cells that may be	example, hyperplasia,
nsed acc	used according to these assays	metaplasia, and/or dysplasia.
may be	may be isolated using	Preferred indications include
techniqu	techniques disclosed herein or	anemia, pancytopenia,
otherwis	otherwise known in the art.	leukopenia, thrombocytopenia,
Human	Human T cells are primary	Hodgkin's disease, acute
human   human	human lymphocytes that	lymphocytic anemia (ALL),
mature i	mature in the thymus and	plasmacytomas, multiple
express		myeloma, Burkitt's lymphoma,
CD3, CI	CD3, CD4, or CD8. These	arthritis, AIDS, granulomatous
cells me	cells mediate humoral or cell-	disease, inflammatory bowel

0.40	4
disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, asthma and allergy.	A preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) TNF alpha production. An alternative preferred embodiment of the invention includes a method for stimulating (e.g., increasing) TNF alpha production. Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"), Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, Crohn"s disease, multiple
mediated immunity and may be preactivated to enhance responsiveness to immunomodulatory factors.	Assays for the activation of transcription through the Serum Response Element (SRE) are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate the serum response factors and modulate the expression of genes involved in growth. Exemplary assays for transcription through the SRE that may be used or routinely modified to test SRE activity of the polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in
	Activation of transcription through serum response element in immune cells (such as T-cells).
	1121
	HELHD85
	173

ificiencies below), nediated	Il-mediated Additional dications ion and rders, and	natoid ional highly n is sepsis. idications diseases	Il below ferative tionally, dications and or example, na, (e.g.,	e, breast, atic, th, brain, uncer. Other is include tive
below), immunodeficiencies (e.g., as described below), boosting a T cell-mediated immune response, and	suppressing a T cell-mediated immune response. Additional highly preferred indications include inflammation and inflammatory disorders, and treating ioint damage in	patients with rheumatoid arthritis. An additional highly preferred indication is sepsis. Highly preferred indications include neoplastic diseases	and/or as described below under "Hyperproliferative Disorders"). Additionally, highly preferred indications include neoplasms and cancers, such as, for example, leukemia, lymphoma, melanoma, glioma (e.g., malignant glioma), solid	tumors, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative
Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al.,	Proc Natl Acad Sci USA 85:6342-6346 (1988); and Black et al., Virus Genes 12(2):105-117 (1997), the content of each of which are herein incorporated by	reference in its entirety. T cells that may be used according to these assays are publicly available (e.g., through the ATCC).	v	
Be (19) Me 368	Prc 85: 85: 812( 12( cor	refe cell acc put thr	may assignment assignment assignment actions actions actions actions actions are actions as a second actions as a second actions as a second actions are actions as a second actions as a second actions as a second action actions as a second action action as a second action actions are a second actions as a second action actions as a second action actions are a second action actions as a second action actions are a second action actions as a second action actions are a second action actions as a second action actions are a second action actions as a second action a	

					disorders and pre-neoplastic
					conditions, such as, for
			-		example, hyperplasia,
	-				metaplasia, and/or dysplasia.
					Preferred indications include
					anemia, pancytopenia,
					leukopenia, thrombocytopenia,
	-				Hodgkin's disease, acute
					lymphocytic anemia (ALL),
					plasmacytomas, multiple
			_		myeloma, Burkitt's lymphoma,
					arthritis, AIDS, granulomatous
					disease, inflammatory bowel
		•			disease, neutropenia,
					neutrophilia, psoriasis,
					suppression of immune
					reactions to transplanted
					organs and tissues,
					hemophilia, hypercoagulation,
					diabetes mellitus, endocarditis,
					meningitis, Lyme Disease,
					cardiac reperfusion injury, and
					asthma and allergy. An
					additional preferred indication
					is infection (e.g., an infectious
<i>,</i> •					disease as described below
					under "Infectious Disease").
	HELHL48	1122	CD152 in Human T		
			Cells		
	HELHL48	1122	Activation or inhibition of	This reporter assay measures activation or inhibition of the	
			T		

et al., Proc Natl Acad Sci USA 85:6342-6346 (1982); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Marone et al, Int Arch Allergy Immunol 114(3):207-17 (1997), the contents of each of which are herein incorporated by reference in its entirety.	Cells were pretreated with SID supernatants or controls for 15-18 hours, and then 10 ng/mL of TNF was added to stimulate the NFkB reporter. SEAP activity was measured after 48 hours. Basophils that may be used according to these assays	are publicly available (e.g., through the ATCC).  Exemplary human basophil cell lines that may be used according to these assays include Ku812, originally established from a patient with	chronic myelogenous leukemia. It is an immature prebasophilic cell line that can be induced to differentiate into mature basophils. See, Kishi et al., Leuk Res. 9:381-390 (1985); Blom et al., Eur J Immunol. 22:2025-32 (1992),

				where the contents of each are	
				herein incorporated by	
				reference in its entirety.	
	HEMAM41	1123	Production of IL-6	IL-6 FMAT. IL-6 is produced	A highly preferred
175				by T cells and has strong	embodiment of the invention
-				effects on B cells. IL-6	includes a method for
				participates in IL-4 induced	stimulating (e.g., increasing)
				IgE production and increases	IL-6 production. An alternative
				IgA production (IgA plays a	highly preferred embodiment
				role in mucosal immunity).	of the invention includes a
				IL-6 induces cytotoxic T cells.	method for inhibiting (e.g.,
				Deregulated expression of IL-6	reducing) IL-6 production. A
				has been linked to autoimmune	highly preferrred indication is
				disease, plasmacytomas,	the stimulation or enhancement
•				myelomas, and chronic	of mucosal immunity. Highly
				hyperproliferative diseases.	preferred indications include
				Assays for immunomodulatory	blood disorders (e.g., as
				and differentiation factor	described below under
		,		proteins produced by a large	"Immune Activity", "Blood-
				variety of cells where the	Related Disorders", and/or
				expression level is strongly	"Cardiovascular Disorders"),
				regulated by cytokines, growth	and infection (e.g., as
				factors, and hormones are well	described below under
				known in the art and may be	"Infectious Disease"). Highly
				used or routinely modified to	preferred indications include
				assess the ability of	autoimmune diseases (e.g.,
				polypeptides of the invention	rheumatoid arthritis, systemic
				(including antibodies and	lupus erythematosis, multiple
				agonists or antagonists of the	sclerosis and/or as described
	·			invention) to mediate	below) and
				immunomodulation and	immunodeficiencies (e.g., as

described below). Highly preferred indications also include boosting a B cell-mediated immune response	and alternatively suppressing a B cell-mediated immune response. Highly preferred	inflammation and	initammatory disorders.Additional highly preferred indications include	asthma and allergy. Highly preferred indications include	neoplastic diseases (e.g., myeloma, plasmacytoma,	leukemia, lymphoma,	melanoma, and/or as described below under	"Hyperproliferative	indications include neoplasms	and cancers, such as, myeloma,	plasmacytoma, leukemia,	prostate, breast, lung, colon,	pancreatic, esophageal,	stomach, brain, liver and		indications include benign	dysproliferative disorders and
differentiation and modulate T cell proliferation and function. Exemplary assays that test for immunomodulatory proteins	evaluate the production of cytokines, such as IL-6, and the stimulation and	upregulation of T cell proliferation and functional	activities. Such assays that may be used or routinely modified to test	immunomodulatory and differentiation activity of	polypeptides of the invention (including antibodies and	agonists or antagonists of the	invention) include assays disclosed in Miraglia et al., J	Biomolecular Screening 4:193-	"Lymphocytes: a practical	approach" Chapter 6:138-160	(2000); and Verhasselt et al., J	(1997), the contents of each of	which are herein incorporated	by reference in its entirety.	Human dendritic cells that may	be used according to these	assavs may be isolated using

				techniques disclosed herein or	pre-neoplastic conditions, such
				otherwise known in the art.	as, for example, hyperplasia,
				Human dendritic cells are	metaplasia, and/or dysplasia.
				antigen presenting cells in	Preferred indications include
				suspension culture, which,	anemia, pancytopenia,
				when activated by antigen	leukopenia, thrombocytopenia,
				and/or cytokines, initiate and	Hodgkin's disease, acute
				upregulate T cell proliferation	lymphocytic anemia (ALL),
				and functional activities.	multiple myeloma, Burkitt's
					lymphoma, arthritis, AIDS,
					granulomatous disease,
					inflammatory bowel disease,
					sepsis, neutropenia,
					neutrophilia, psoriasis,
					suppression of immune
					reactions to transplanted
-					organs and tissues,
					hemophilia, hypercoagulation,
					diabetes mellitus, endocarditis,
					meningitis, and Lyme Disease.
					An additonal preferred
					indication is infection (e.g., an
					infectious disease as described
					below under "Infectious
					Disease").
	HEMAM41	1123	Production of TNF	TNFa FMAT. Assays for	A highly preferred
175			alpha by dendritic	immunomodulatory proteins	embodiment of the invention
			cells	produced by activated	includes a method for
				macrophages, T cells,	inhibiting (e.g., decreasing)
				fibroblasts, smooth muscle,	TNF alpha production. An
				and other cell types that exert a	alternative highly preferred

, F 0 B	, F 0 B	E 09 E 75 77	embodiment of the invention	includes a method for	stimulating (e.g., increasing)	TNF alpha production.	Highly preferred indications	include blood disorders (e.g.,	as described below under	"Immune Activity", "Blood-	Related Disorders", and/or	"Cardiovascular Disorders"),	Highly preferred indications	include autoimmune diseases	(e.g., rheumatoid arthritis,	systemic lupus erythematosis,	Crohn"s disease, multiple	sclerosis and/or as described	below), immunodeficiencies	(e.g., as described below),	boosting a T cell-mediated	immune response, and	suppressing a T cell-mediated	immune response. Additional	highly preferred indications	include inflammation and	inflammatory disorders, and	treating joint damage in	patients with rheumatoid	arthritis. An additional highly	preferred indication is sensis	protection marginary to achoro.
						_				or																						

					reactions to transplanted
					organs and tissues,
					hemophilia, hypercoagulation,
					diabetes mellitus, endocarditis,
					meningitis, Lyme Disease,
					cardiac reperfusion injury, and
					asthma and allergy. An
					additional preferred indication
					is infection (e.g., an infectious
					disease as described below
					under "Infectious Disease").
	HEPAA46	1124	Activation of	Assays for the activation of	A preferred embodiment of
176			transcription	transcription through the	the invention includes a
	-		through serum	Serum Response Element	method for inhibiting (e.g.,
			response element in	(SRE) are well-known in the	reducing) TNF alpha
			immune cells (such	art and may be used or	production. An alternative
			as T-cells).	routinely modified to assess	preferred embodiment of the
				the ability of polypeptides of	invention includes a method
				the invention (including	for stimulating (e.g.,
			-	antibodies and agonists or	increasing) TNF alpha
				antagonists of the invention) to	production. Preferred
				regulate the serum response	indications include blood
				factors and modulate the	disorders (e.g., as described
				expression of genes involved	below under "Immune
				in growth. Exemplary assays	Activity", "Blood-Related
				for transcription through the	Disorders", and/or
				SRE that may be used or	"Cardiovascular Disorders"),
				routinely modified to test SRE	Highly preferred indications
				activity of the polypeptides of	include autoimmune diseases
				the invention (including	(e.g., rheumatoid arthritis,
				antibodies and agonists or	systemic lupus erythematosis,

		antagonists of the invention)	Crohn"s disease, multiple
		include assays disclosed in	sclerosis and/or as described
		Berger et al., Gene 66:1-10	below), immunodeficiencies
 		(1998); Cullen and Malm,	(e.g., as described below),
 		Methods in Enzymol 216:362-	boosting a T cell-mediated
 		368 (1992); Henthorn et al.,	immune response, and
		Proc Natl Acad Sci USA	suppressing a T cell-mediated
		85:6342-6346 (1988); and	immune response. Additional
		Black et al., Virus Genes	highly preferred indications
		12(2):105-117 (1997), the	include inflammation and
		content of each of which are	inflammatory disorders, and
		herein incorporated by	treating joint damage in
		reference in its entirety. T	patients with rheumatoid
		cells that may be used	arthritis. An additional highly
	-	according to these assays are	preferred indication is sepsis.
		publicly available (e.g.,	Highly preferred indications
		through the ATCC).	include neoplastic diseases
 		Exemplary mouse T cells that	(e.g., leukemia, lymphoma,
		may be used according to these	and/or as described below
 		assays include the CTLL cell	under "Hyperproliferative
		line, which is an IL-2	Disorders"). Additionally,
 		dependent suspension culture	highly preferred indications
		of T cells with cytotoxic	include neoplasms and
		activity.	cancers, such as, for example,
			leukemia, lymphoma,
			melanoma, glioma (e.g.,
			malignant glioma), solid
			tumors, and prostate, breast,
			lung, colon, pancreatic,
			esophageal, stomach, brain,
 			liver and urinary cancer. Other

	HEPAA46	1124	IL-2 in Human T-		
176			cell 2B9		
	HEPAB80	1125	Activation of	Kinase assay. Kinase assays,	A highly preferred
177			Adipocyte ERK	for example an Elk-1 kinase	embodiment of the invention
			Signaling Pathway	assay, for ERK signal	includes a method for
				transduction that regulate cell	stimulating adipocyte
				proliferation or differentiation	proliferation. An alternative
				are well known in the art and	highly preferred embodiment
				may be used or routinely	of the invention includes a
				modified to assess the ability	method for inhibiting
				of polypeptides of the	adipocyte proliferation. A
				invention (including antibodies	highly preferred embodiment
				and agonists or antagonists of	of the invention includes a
				the invention) to promote or	method for stimulating
				inhibit cell proliferation,	adipocyte differentiation. An
10				activation, and differentiation.	alternative highly preferred
				Exemplary assays for ERK	embodiment of the invention
				kinase activity that may be	includes a method for
				used or routinely modified to	inhibiting adipocyte
				test ERK kinase-induced	differentiation. A highly
				activity of polypeptides of the	preferred embodiment of the
				invention (including antibodies	invention includes a method
				and agonists or antagonists of	for stimulating (e.g.,
<u> </u>				the invention) include the	increasing) adipocyte
				assays disclosed in Forrer et	activation. An alternative
				al., Biol Chem 379(8-9):1101-	highly preferred embodiment
				1110 (1998); Le Marchand-	of the invention includes a
				Brustel Y, Exp Clin	method for inhibiting the
				Endocrinol Diabetes	activation of (e.g., decreasing)
	-			107(2):126-132 (1999);	and/or inactivating adipocytes.
				Kyriakis JM, Biochem Soc	Highly preferred indications

Symp 64:29-48 (1999); Chang and Karin, Nature 410(6824):37-40 (2001); and Cobb MH, Prog Biophys Mol Biol 71(3-4):479-500 (1999); the contents of each of which are herein incorporated by reference in its entirety. Mouse adipocyte cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary mouse adipocyte cells that may be used cocording to these assays include 3T3-L1 cells 3T3-L1 is an adherent mouse preadipocyte cell line that is a continuous substrain of 3T3 fibroblast cells developed through clonal isolation and undergo a pre-adipocyte to adipose-like conversion under conditions known in the art.  A highly preferred indications include are below under "Endocrine Disorders".  Highly preferred indications as described below under "Immune Activity", and/or "Blood-Related blisorders", immune disorders (e.g., as described below under "Immune Activity"), neural adipose-like conversion under appropriate differentiation and infection (e.g., as described below under "Immune Activity"), neural adipose-like conversion under "Immune Activity"), and highly preferred indication "Immune Activity"), and highly preferred indication  A highly preferred indication	Chang ); and ss Mol 1999); which by to these lable C). ocyte sat is a 3T3 ed t and e to t under ion e art.	Chang  Chang  Shall  Sh
Symp 64:29-2 and Karin, Ne 410(6824):37 Cobb MH, Pr Biol 71(3-4):4 the contents of are herein inc reference in it Mouse adipoce may be used a assays are pul (e.g., through Exemplary m cells that may according to t include 3T3-I is an adherent preadipocyte continuous su fibroblast cell through clona undergo a pre adipose-like c appropriate di conditions kn	Symp 64:29- and Karin, Ng 410(6824):37 Cobb MH, Pr Biol 71(3-4): the contents o are herein inc reference in it Mouse adipoc may be used a assays are pul (e.g., through Exemplary m cells that may according to t include 3T3-I is an adherent preadipocyte continuous su fibroblast cell through clona undergo a pre adipose-like c appropriate di conditions kn	and Karin, Ng 410(6824):37 Cobb MH, Pr Biol 71(3-4):4 He contents of are herein inc reference in it Mouse adipoc may be used a assays are pul (e.g., through Exemplary m cells that may according to t include 3T3-1 is an adherent preadipocyte continuous su fibroblast cell through clona undergo a pre adipose-like c appropriate di conditions kn

indication is a complication	associated with diabetes (e.g.,	diabetic retinopathy, diabetic	nephropathy, kidney disease	(e.g., renal failure,	nephropathy and/or other	diseases and disorders as	described in the "Renal	Disorders" section below),	diabetic neuropathy, nerve	disease and nerve damage	(e.g., due to diabetic	neuropathy), blood vessel	blockage, heart disease, stroke,	impotence (e.g., due to diabetic	neuropathy or blood vessel	blockage), seizures, mental	confusion, drowsiness,	nonketotic hyperglycemic-	hyperosmolar coma,	cardiovascular disease (e.g.,	heart disease, atherosclerosis,	microvascular disease,	hypertension, stroke, and other	diseases and disorders as	described in the	"Cardiovascular Disorders"	section below), dyslipidemia,	endocrine disorders (as	described in the "Endocrine	Disorders" section below),
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neuropathy, vision impairment	(e.g., diabetic retinopathy and	blindness), ulcers and impaired	wound healing, infection (e.g.,	infectious diseases and	disorders as described in the	"Infectious Diseases" section	below (particularly of the	urinary tract and skin). An	additional highly preferred	indication is obesity and/or	complications associated with	obesity. Additional highly	preferred indications include	weight loss or alternatively,	weight gain. Additional	highly preferred indications are	complications associated with	insulin resistance.	Additional highly preferred	indications are disorders of the	musculoskeletal systems	including myopathies,	muscular dystrophy, and/or as	described herein.	Additional highly preferred	indications include,	hypertension, coronary artery	disease, dyslipidemia,	gallstones, osteoarthritis,	degenerative arthritic esting
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					disorders, fibrosis, cachexia, and kidney diseases or disorders. Preferred indications include neoplasms and cancer, such as, lymphoma, leukemia and breast, colon, and kidney cancer. Additional preferred indications include melanoma, prostate, lung, pancreatic, esophageal, stomach, brain, liver, and urinary cancer. Highly preferred indications include lipomas and liposarcomas. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia,
177	HEPAB80	1125	Regulation of viability and proliferation of pancreatic beta cells.	Assays for the regulation of viability and proliferation of cells in vitro are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate viability and proliferation of pancreatic beta	A highly preferred indication is diabetes mellitus. An additional highly preferred indication associated with diabetes (e.g., diabetic retinopathy, diabetic nephropathy, kidney disease (e.g., renal failure, nephropathy and/or other diseases and disorders as described in the "Renal

cells. For example, the Cell	Disorders" section below),
Titer-Glo luminescent cell	diabetic neuropathy, nerve
viability assay measures the	disease and nerve damage
number of viable cells in	(e.g., due to diabetic
culture based on quantitation	neuropathy), blood vessel
of the ATP present which	blockage, heart disease, stroke,
signals the presence of	impotence (e.g., due to diabetic
metabolically active cells.	neuropathy or blood vessel
Exemplary assays that may be	blockage), seizures, mental
used or routinely modified to	confusion, drowsiness,
test regulation of viability and	nonketotic hyperglycemic-
proliferation of pancreatic beta	hyperosmolar coma,
cells by polypeptides of the	cardiovascular disease (e.g.,
invention (including antibodies	heart disease, atherosclerosis,
and agonists or antagonists of	microvascular disease,
the invention) include assays	hypertension, stroke, and other
disclosed in: Ohtani KI, et al.,	diseases and disorders as
Endocrinology, 139(1):172-8	described in the
(1998); Krautheim A, et al,	"Cardiovascular Disorders"
Exp Clin Endocrinol Diabetes,	section below), dyslipidemia,
107 (1):29-34 (1999), the	endocrine disorders (as
contents of each of which is	described in the "Endocrine
herein incorporated by	Disorders" section below),
reference in its entirety.	neuropathy, vision impairment
Pancreatic cells that may be	(e.g., diabetic retinopathy and
used according to these assays	blindness), ulcers and impaired
are publicly available (e.g.,	wound healing, and infection
through the ATCC) and/or	(e.g., infectious diseases and
may be routinely generated.	disorders as described in the
Exemplary pancreatic cells that	"Infectious Diseases" section
 may be used according to these	below, especially of the

				assays include HITT15 Cells. HITT15 are an adherent epithelial cell line established from Syrian hamster islet cells transformed with SV40. These cells express glucagon, somatostatin, and glucocorticoid receptors. The cells secrete insulin, which is stimulated by glucose and glucagon and suppressed by somatostatin or glucocorticoids. ATTC# CRL-177 Refs: Lord and Ashcroft. Biochem. J. 219: 547-551; Santerre et al. Proc. Natl. Acad. Sci. USA 78: 4339-4343, 1981.	urinary tract and skin), carpal tunnel syndrome and Dupuytren's contracture). An additional highly preferred indication is obesity and/or complications associated with obesity. Additional highly preferred indications include weight loss or alternatively, weight gain. Additional highly preferred indications are complications associated with insulin resistance.
177	HEPAB80	1125	IL-6 in HUVEC		
178	HEQAK71	1126	Production of TNF alpha by dendritic cells	TNFa FMAT. Assays for immunomodulatory proteins produced by activated macrophages, T cells, fibroblasts, smooth muscle, and other cell types that exert a wide variety of inflammatory and cytotoxic effects on a variety of cells are well known in the art and may be used or routinely modified to assess	A highly preferred embodiment of the invention includes a method for inhibiting (e.g., decreasing) TNF alpha production. An alternative highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing) TNF alpha production. Highly preferred indications

	the shility of nolynewides of include blood disorders (e.g.		ıc	n) to		modulate inflammation and Highly preferred indications	cytotoxicity. Exemplary include autoimmune diseases	assays that test for (e.g., rheumatoid arthritis,	immunomodulatory proteins systemic lupus erythematosis,	evaluate the production of Crohn's disease, multiple	cytokines such as tumor sclerosis and/or as described	necrosis factor alpha (TNFa), below), immunodeficiencies	and the induction or inhibition (e.g., as described below),	of an inflammatory or boosting a T cell-mediated	cytotoxic response. Such immune response, and	assays that may be used or suppressing a T cell-mediated	routinely modified to test immune response. Additional	<u></u>	polypeptides of the invention include inflammation and	(including antibodies and inflammatory disorders, and	agonists or antagonists of the treating joint damage in	invention) include assays patients with rheumatoid	disclosed in Miraglia et al., J arthritis. An additional highly	Biomolecular Screening 4:193- preferred indication is sepsis.	204(1999); Rowland et al., Highly preferred indications		approach" Chapter 6:138-160 (e.g., leukemia, lymphoma,	(2000); Verhasselt et al., Eur J and/or as described below	Immunol 28(11):3886-3890   under "Hyperproliferative	(1198); Dahlen et al., J Disorders"). Additionally,
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include neoplasms and	cancers, such as, leukemia,	lymphoma, melanoma, glioma	(e.g., malignant glioma), solid	tumors, and prostate, breast,	lung, colon, pancreatic,	esophageal, stomach, brain,		preferred indications include	benign dysproliferative	disorders and pre-neoplastic	conditions, such as, for	example, hyperplasia,	metaplasia, and/or dysplasia.	Preferred indications include	anemia, pancytopenia,	leukopenia, thrombocytopenia,	Hodgkin's disease, acute	lymphocytic anemia (ALL),	plasmacytomas, multiple	myeloma, Burkitt's lymphoma,	arthritis, AIDS, granulomatous	disease, inflammatory bowel	disease, neutropenia,	neutrophilia, psoriasis,	suppression of immune	reactions to transplanted	organs and tissues,	hemophilia, hypercoagulation,	diabetes mellitus, endocarditis,	meningitis, Lyme Disease,
(1998); Verhasselt et al., J	158:2919-2925	(1997); and Nardelli et al., J	Leukoc Biol 65:822-828	(1999), the contents of each of	which are herein incorporated	by reference in its entirety.	Human dendritic cells that may	be used according to these	assays may be isolated using	techniques disclosed herein or	otherwise known in the art.	Human dendritic cells are	antigen presenting cells in	suspension culture, which,	when activated by antigen	and/or cytokines, initiate and	upregulate T cell proliferation	and functional activities.											,	
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					cardiac reperfusion injury, and asthma and allergy. An additional preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease").
178	HEQAK71	1126	Production of ICAM-1	Assays for measuring expression of ICAM-1 are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate ICAM-1 expression. Exemplary assays that may be used or routinely modified to measure ICAM-1 expression include assays disclosed in: Takacs P, et al, FASEB J, 15(2):279-281 (2001); and, Miyamoto K, et al., Am J Pathol, 156(5):1733-1739 (2000), the contents of each of which is herein incorporated by reference in its entirety. Cells that may be used according to these assays are publicly available (e.g.,	Preferred embodiments of the invention include using polypeptides of the invention (or antibodies, agonists, or antagonists thereof) in detection, diagnosis, prevention, and/or treatment of Inflammation, Vascular Disease, Athereosclerosis, Restenosis, and Stroke
				through the ATCC) and/or may be routinely generated.	

				Exemplary cells that may be used according to these assays	
				include microvascular endothelial cells (MVEC).	
	HERAR44	1127	Activation of	This reporter assay measures	Highly preferred indication
179			transcription	activation of the NFkB	includes allergy, asthma, and
			through NFKB	signaling pathway in Ku812	rhinitis. Additional highly
			response element in	human basophil cell line.	preferred indications include
			immune cells (such	Assays for the activation of	infection (e.g., an infectious
			as basophils).	transcription through the	disease as described below
				NFKB response element are	under "Infectious Disease"),
				well-known in the art and may	and inflammation and
				be used or routinely modified	inflammatory disorders.
				to assess the ability of	Preferred indications include
				polypeptides of the invention	immunological and
				(including antibodies and	hempatopoietic disorders (e.g.,
		·		agonists or antagonists of the	as described below under
				invention) to regulate NFKB	"Immune Activity", and
				transcription factors and	"Blood-Related Disorders").
				modulate expression of	Preferred indications also
			-	immunomodulatory genes.	include autoimmune diseases
	_ <del>-</del>	-		Exemplary assays for	(e.g., rheumatoid arthritis,
				transcription through the	systemic lupus erythematosis,
				NFKB response element that	multiple sclerosis and/or as
	-			may be used or rountinely	described below) and
				modified to test NFKB-	immunodeficiencies (e.g., as
		18		response element activity of	described below). Preferred
				polypeptides of the invention	indications also include
				(including antibodies and	neoplastic diseases (e.g.,
				agonists or antagonists of the	leukemia, lymphoma,
				invention) include assays	melanoma, and/or as described

				disclosed in Berger et al., Gene	below under
				66:1-10 (1998); Cullen and	"Hyperproliferative
-				Malm, Methods in Enzymol	Disorders"). Preferred
				216:362-368 (1992); Henthorn	indications include neoplasms
-				et al., Proc Natl Acad Sci USA	and cancer, such as, for
				85:6342-6346 (1988); Marone	example, leukemia, lymphoma,
				et al, Int Arch Allergy	melanoma, and prostate,
				Immunol 114(3):207-17	breast, lung, colon, pancreatic,
				(1997), the contents of each of	esophageal, stomach, brain,
				which are herein incorporated	liver, urinary tract cancers and
				by reference in its entirety.	as described below under
				Basophils that may be used	"Hyperproliferative
				according to these assays are	Disorders".
				publicly available (e.g.,	
				through the ATCC).	
				Exemplary human basophil	
				cell lines that may be used	
				according to these assays	
				include Ku812, originally	
				established from a patient with	
				chronic myelogenous	
				leukemia. It is an immature	
				prebasophilic cell line that can	
				be induced to differentiate into	
				mature basophils.	
	HERAR44	1127	Production of	Assays for measuring	Preferred embodiments of the
179			ICAM-1	expression of ICAM-1 are	invention include using
				well-known in the art and may	polypeptides of the invention
				be used or routinely modified	(or antibodies, agonists, or
				to assess the ability of	antagonists thereof) in
				polypeptides of the invention	detection, diagnosis,

				(including antibodies and	prevention, and/or treatment of
				agonists or antagonists of the	Inflammation, Vascular
				invention) to regulate ICAM-1	Disease, Athereosclerosis,
				expression. Exemplary assays	Restenosis, and Stroke
				that may be used or routinely	
				modified to measure ICAM-1	
				expression include assays	
				disclosed in: Takacs P, et al,	
				FASEB J, 15(2):279-281	
				(2001); and, Miyamoto K, et	
				al., Am J Pathol, 156(5):1733-	
				1739 (2000), the contents of	
				each of which is herein	
				incorporated by reference in its	
				entirety. Cells that may be	
				used according to these assays	
				are publicly available (e.g.,	
				through the ATCC) and/or	
	-			may be routinely generated.	
				Exemplary cells that may be	
				used according to these assays	
				include microvascular	
				endothelial cells (MVEC).	
	HESAJ10	1128	Regulation of	Caspase Apoptosis. Assays for	Preferred embodiments of the
180			apoptosis of	caspase apoptosis are well	invention include using
			immune cells (such	known in the art and may be	polypeptides of the invention
			as mast cells).	used or routinely modified to	(or antibodies, agonists, or
				assess the ability of	antagonists thereof) in
	-			polypeptides of the invention	detection, diagnosis,
				(including antibodies and	prevention, and/or treatment of
				agonists or antagonists of the	asthma, allergy,

hypersensitivity and	inflammation.																													
invention) to regulate caspase	protease-mediated apoptosis in	immune cells (such as, for	example, in mast cells). Mast	cells are found in connective	and mucosal tissues throughout	the body, and their activation	via immunoglobulin E -	antigen, promoted by T helper	cell type 2 cytokines, is an	important component of	allergic disease. Dysregulation	of mast cell apoptosis may	play a role in allergic disease	and mast cell tumor survival.	Exemplary assays for caspase	apoptosis that may be used or	routinely modified to test	capase apoptosis activity	induced by polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) include the	assays disclosed in: Masuda A,	et al., J Biol Chem,	276(28):26107-26113 (2001);	Yeatman CF 2nd, et al., J Exp	Med, 192(8):1093-1103	(2000);Lee et al., FEBS Lett	485(2-3): 122-126 (2000); Nor	et al., J Vasc Res 37(3): 209-
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218 (2000); and Karsan and Harlan, J Atheroscler Thromb 3(2): 75-80 (1996); the contents of each of which are herein incorporated by reference in its entirety. Immune cells that may be used according to these assays are publicly available (e.g., through commercial sources). Exemplary immune cells that may be used according to these assays include mast cells such as the HMC human mast cell line.	This reporter assay measures activation or inhibition of the NFkB signaling pathway in Ku812 human basophil cell line. Assays for the activation or inhibition of transcription through the NFKB response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate NFKB transcription factors and modulate
	Activation or inhibition of transcription transcription through NFKB response element in immune cells (such as basophils).
	1129
	HETAB45
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expression of	immunomodulatory genes.	NFkB is important in the	pathogenesis of asthma.	Exemplary assays for	transcription through the	NFKB response element that	may be used or rountinely	modified to test NFKB-	response element activity of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include assays	disclosed in Berger et al., Gene	66:1-10 (1998); Cullen and	Malm, Methods in Enzymol	216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA	85:6342-6346 (1988); Marone	et al, Int Arch Allergy	Immunol 114(3):207-17	(1997), the contents of each of	which are herein incorporated	by reference in its entirety.	Cells were pretreated with SID	supernatants or controls for 15-	18 hours, and then 10 ng/mL	of TNF was added to stimulate	the NFkB reporter. SEAP	activity was measured after 48
										-	-														-					

modulate expression of	immunomodulatory genes.	Exemplary assays for	transcription through the	NFKB response element that	may be used or rountinely	modified to test NFKB-	response element activity of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include assays	disclosed in: Gri G, et al., Biol	Chem, 273(11):6431-6438	(1998); Pyatt DW, et al., Cell	Biol Toxicol 2000;16(1):41-51	(2000); Berger et al., Gene	66:1-10 (1998); Cullen and	Malm, Methods in Enzymol	216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA	85:6342-6346 (1988); Valle	Blazquez et al, Immunology	90(3):455-460 (1997);	Aramburau et al., J Exp Med	82(3):801-810 (1995); and	Fraser et al., 29(3):838-844	(1999), the contents of each of	which are herein incorporated	by reference in its entirety.	Immune cells that may be used
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ure hat these cell	may polypeptides of the invention include using may polypeptides of the invention iced (or antibodies, agonists, or antagonists thereof) in detection, diagnosis, prevention, and/or treatment of Inflammation, Vascular M-1 Disease, Athereosclerosis, says Restenosis, and Stroke et 733- of says.
according to these assays are publicly available (e.g., through the ATCC).  Exemplary immune cells that may be used according to these assays include the Reh B-cell line.	Assays for measuring expression of ICAM-1 are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate ICAM-1 expression. Exemplary assays that may be used or routinely modified to measure ICAM-1 expression include assays disclosed in: Takacs P, et al, FASEB J, 15(2):279-281 (2001); and, Miyamoto K, et al., Am J Pathol, 156(5):1733-1739 (2000), the contents of each of which is herein incorporated by reference in its entirety. Cells that may be used according to these assays are publicly available (e.g., through the ATCC) and/or
	IT30 Production of ICAM-1
	HETBR16 11
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				may be routinely generated.  Exemplary cells that may be	
				used according to these assays include microvascular endothelial cells (MVEC).	
182	HETBR16	1130	SEAP in OE-21		
	HETLM70	1131	Production of IL-6	IL-6 FMAT. IL-6 is produced	A highly preferred
183				by T cells and has strong	embodiment of the invention
				effects on B cells. IL-6	includes a method for
				participates in IL-4 induced	stimulating (e.g., increasing)
				IgE production and increases	IL-6 production. An alternative
				IgA production (IgA plays a	highly preferred embodiment
				role in mucosal immunity).	of the invention includes a
				IL-6 induces cytotoxic T cells.	method for inhibiting (e.g.,
				Deregulated expression of IL-6	reducing) IL-6 production. A
				has been linked to autoimmune	highly preferrred indication is
				disease, plasmacytomas,	the stimulation or enhancement
				myelomas, and chronic	of mucosal immunity. Highly
				hyperproliferative diseases.	preferred indications include
				Assays for immunomodulatory	blood disorders (e.g., as
				and differentiation factor	described below under
				proteins produced by a large	"Immune Activity", "Blood-
				variety of cells where the	Related Disorders", and/or
				expression level is strongly	"Cardiovascular Disorders"),
				regulated by cytokines, growth	and infection (e.g., as
				factors, and hormones are well	described below under
				known in the art and may be	"Infectious Disease"). Highly
				used or routinely modified to	preferred indications include
				assess the ability of	autoimmune diseases (e.g.,
				polypeptides of the invention	rheumatoid arthritis, systemic

lupus erythematosis, multiple	sclerosis and/or as described	below) and	immunodeficiencies (e.g., as	described below). Highly	preferred indications also	include boosting a B cell-	mediated immune response	and alternatively suppressing a	B cell-mediated immune	response. Highly preferred	indications include	inflammation and	inflammatory	disorders. Additional highly	preferred indications include	asthma and allergy. Highly	preferred indications include	neoplastic diseases (e.g.,	myeloma, plasmacytoma,	leukemia, lymphoma,	melanoma, and/or as described	below under	"Hyperproliferative	Disorders"). Highly preferred	indications include neoplasms	and cancers, such as, myeloma,	plasmacytoma, leukemia,	lymphoma, melanoma, and	prostate, breast, lung, colon,	pancreatic, esophageal,
(including antibodies and	agonists or antagonists of the	invention) to mediate	immunomodulation and	differentiation and modulate T	cell proliferation and function.	Exemplary assays that test for	immunomodulatory proteins	evaluate the production of	cytokines, such as IL-6, and	the stimulation and	upregulation of T cell	proliferation and functional	activities. Such assays that	may be used or routinely	modified to test	immunomodulatory and	diffferentiation activity of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include assays	disclosed in Miraglia et al., J	Biomolecular Screening 4:193-	204(1999); Rowland et al.,	"Lymphocytes: a practical	approach" Chapter 6:138-160	(2000); and Verhasselt et al., J	Immunol 158:2919-2925	(1997), the contents of each of	which are herein incorporated
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				by reference in its entirety.	stomach, brain, liver and
	<u>-</u>			Human dendritic cells that may	urinary cancer. Other preferred
				be used according to these	indications include benign
				assays may be isolated using	dysproliferative disorders and
				techniques disclosed herein or	pre-neoplastic conditions, such
				otherwise known in the art.	as, for example, hyperplasia,
		-14		Human dendritic cells are	metaplasia, and/or dysplasia.
				antigen presenting cells in	Preferred indications include
		-		suspension culture, which,	anemia, pancytopenia,
				when activated by antigen	leukopenia, thrombocytopenia,
				and/or cytokines, initiate and	Hodgkin's disease, acute
				upregulate T cell proliferation	lymphocytic anemia (ALL),
				and functional activities.	multiple myeloma, Burkitt's
					lymphoma, arthritis, AIDS,
					granulomatous disease,
					inflammatory bowel disease,
					sepsis, neutropenia,
					neutrophilia, psoriasis,
					suppression of immune
					reactions to transplanted
					organs and tissues,
					hemophilia, hypercoagulation,
					diabetes mellitus, endocarditis,
					meningitis, and Lyme Disease.
					An additonal preferred
					indication is infection (e.g., an
					infectious disease as described
					below under "Infectious
		!	 		Disease").
	HETLM70	1131	Production of	MIP-1alpha FMAT. Assays	A highly preferred
183			MIPlalpha	for immunomodulatory	embodiment of the invention

	proteins	proteins produced by activated	includes a method for
	dendritic	dendritic cells that upregulate	stimulating MIP1a production.
	monocyt	monocyte/macrophage and T	An alternative highly preferred
	cell chem	cell chemotaxis are well	embodiment of the invention
	known in	known in the art and may be	includes a method for
	used or r	used or routinely modified to	inhibiting (e.g., reducing)
	assess the	assess the ability of	MIP1a production. A highly
	polypept	polypeptides of the invention	preferred indication is
	(includin	(including antibodies and	infection (e.g., an infectious
	agonists	agonists or antagonists of the	disease as described below
	inventior	invention) to mediate	under "Infectious Disease").
		immunomodulation, modulate	Preferred indications include
	chemotax	chemotaxis, and modulate T	blood disorders (e.g., as
	cell diffe	cell differentiation. Exemplary	described below under
	assays th	assays that test for	"Immune Activity", "Blood-
<u>.</u>	ionnumi	immunomodulatory proteins	Related Disorders", and/or
	evaluate	evaluate the production of	"Cardiovascular Disorders").
	chemokii	chemokines, such as	Highly preferred indications
	macroph	macrophage inflammatory	include autoimmune diseases
	protein 1	protein 1 alpha (MIP-1a), and	(e.g., rheumatoid arthritis,
	the activa	the activation of	systemic lupus erythematosis,
	monocyt	monocytes/macrophages and T	multiple sclerosis and/or as
	cells. Su	cells. Such assays that may be	described below) and
	used or r	used or routinely modified to	immunodeficiencies (e.g., as
	test imm	test immunomodulatory and	described below). Additional
-	chemota	chemotaxis activity of	highly preferred indications
	polypept	polypeptides of the invention	include inflammation and
	(includin	(including antibodies and	inflammatory disorders.
	agonists	agonists or antagonists of the	Preferred indications also
	inventior	invention) include assays	include anemia, pancytopenia,
	disclosed	disclosed in Miraglia et al., J	leukopenia, thrombocytopenia,

	Biomolecular Screening 4:193-	Hodgkin's disease, acute
	204(1999); Rowland et al.,	lymphocytic anemia (ALL),
	"Lymphocytes: a practical	plasmacytomas, multiple
	approach" Chapter 6:138-160	myeloma, Burkitt's lymphoma,
	(2000); Satthaporn and	arthritis, AIDS, granulomatous
	Eremin, J R Coll Surg Ednb	disease, inflammatory bowel
	45(1):9-19 (2001); Drakes et	disease, sepsis, neutropenia,
	al., Transp Immunol 8(1):17-	neutrophilia, psoriasis,
	29 (2000); Verhasselt et al., J	suppression of immune
	Immunol 158:2919-2925	reactions to transplanted
	(1997); and Nardelli et al., J	organs and tissues, hemophilia,
	Leukoc Biol 65:822-828	hypercoagulation, diabetes
	(1999), the contents of each of	mellitus, endocarditis,
	which are herein incorporated	meningitis, Lyme Disease,
-	by reference in its entirety.	asthma, and allergy.
	Human dendritic cells that may	Preferred indications also
	be used according to these	include neoplastic diseases
	assays may be isolated using	(e.g., leukemia, lymphoma,
	techniques disclosed herein or	and/or as described below
	otherwise known in the art.	under "Hyperproliferative
	Human dendritic cells are	Disorders"). Highly preferred
	antigen presenting cells in	indications include neoplasms
	suspension culture, which,	and cancers, such as, leukemia,
	when activated by antigen	lymphoma, prostate, breast,
	and/or cytokines, initiate and	lung, colon, pancreatic,
	upregulate T cell proliferation	esophageal, stomach, brain,
	and functional activities.	liver, and urinary cancer. Other
		preferred indications include
		benign dysproliferative
		disorders and pre-neoplastic
		conditions, such as, for

					example, hyperplasia,
					metaplasia, and/or dysplasia.
1 1	HETLM70	1131	Production of TNF	TNFa FMAT. Assays for	A highly preferred
183			alpha by dendritic	immunomodulatory proteins	embodiment of the invention
			cells	produced by activated	includes a method for
				macrophages, T cells,	inhibiting (e.g., decreasing)
				fibroblasts, smooth muscle,	TNF alpha production. An
				and other cell types that exert a	alternative highly preferred
				wide variety of inflammatory	embodiment of the invention
				and cytotoxic effects on a	includes a method for
				variety of cells are well known	stimulating (e.g., increasing)
				in the art and may be used or	TNF alpha production.
				routinely modified to assess	Highly preferred indications
		- <del></del>		the ability of polypeptides of	include blood disorders (e.g.,
				the invention (including	as described below under
				antibodies and agonists or	"Immune Activity", "Blood-
				antagonists of the invention) to	Related Disorders", and/or
				mediate immunomodulation,	"Cardiovascular Disorders"),
				modulate inflammation and	Highly preferred indications
				cytotoxicity. Exemplary	include autoimmune diseases
				assays that test for	(e.g., rheumatoid arthritis,
				immunomodulatory proteins	systemic lupus erythematosis,
				evaluate the production of	Crohn's disease, multiple
				cytokines such as tumor	sclerosis and/or as described
				necrosis factor alpha (TNFa),	below), immunodeficiencies
				and the induction or inhibition	(e.g., as described below),
				of an inflammatory or	boosting a T cell-mediated
				cytotoxic response. Such	immune response, and
				assays that may be used or	suppressing a T cell-mediated
				routinely modified to test	immune response. Additional
				immunomodulatory activity of	highly preferred indications

	nolymentides of the invention	include inflammation and
	fincluding antihodies and	inflammatory disorders and
	agonists or antagonists of the	treating joint damage in
	invention) include assays	patients with rheumatoid
	disclosed in Miraglia et al., J	arthritis. An additional highly
	Biomolecular Screening 4:193-	preferred indication is sepsis.
	204(1999); Rowland et al.,	Highly preferred indications
	"Lymphocytes: a practical	include neoplastic diseases
	approach" Chapter 6:138-160	(e.g., leukemia, lymphoma,
	(2000); Verhasselt et al., Eur J	and/or as described below
	Immunol 28(11):3886-3890	under "Hyperproliferative
	(1198); Dahlen et al., J	Disorders"). Additionally,
	Immunol 160(7):3585-3593	highly preferred indications
	(1998); Verhasselt et al., J	include neoplasms and
	Immunol 158:2919-2925	cancers, such as, leukemia,
	(1997); and Nardelli et al., J	lymphoma, melanoma, glioma
	Leukoc Biol 65:822-828	(e.g., malignant glioma), solid
	(1999), the contents of each of	tumors, and prostate, breast,
	which are herein incorporated	lung, colon, pancreatic,
	by reference in its entirety.	esophageal, stomach, brain,
	Human dendritic cells that may	liver and urinary cancer. Other
	be used according to these	preferred indications include
	assays may be isolated using	benign dysproliferative
	techniques disclosed herein or	disorders and pre-neoplastic
	otherwise known in the art.	conditions, such as, for
	Human dendritic cells are	example, hyperplasia,
	antigen presenting cells in	metaplasia, and/or dysplasia.
	suspension culture, which,	Preferred indications include
	when activated by antigen	anemia, pancytopenia,
	and/or cytokines, initiate and	leukopenia, thrombocytopenia,
	upregulate T cell proliferation	Hodgkin's disease, acute

				and functional activities.	lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, cardiac reperfusion injury, and asthma and allergy. An additional preferred indication is infection (e.g., an infectious disease as described below
183	HETLM70	1131	SEAP in HIB/CRE		under "Infectious Disease").
184	HFABG18	1132	Activation of Adipocyte ERK Signaling Pathway	Kinase assay. Kinase assays, for example an Elk-1 kinase assay, for ERK signal transduction that regulate cell proliferation or differentiation are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the	A highly preferred embodiment of the invention includes a method for stimulating adipocyte proliferation. An alternative highly preferred embodiment of the invention includes a method for inhibiting adipocyte proliferation. A

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of the invention includes a	method for stimulating	adipocyte differentiation. An	alternative highly preferred	embodiment of the invention	includes a method for	inhibiting adipocyte	differentiation. A highly	preferred embodiment of the	invention includes a method	for stimulating (e.g.,	increasing) adipocyte	activation. An alternative	highly preferred embodiment	of the invention includes a	method for inhibiting the	activation of (e.g., decreasing)	and/or inactivating adipocytes.	Highly preferred indications	include endocrine disorders	(e.g., as described below under	"Endocrine Disorders").	Highly preferred indications	also include neoplastic	diseases (e.g., lipomas,	liposarcomas, and/or as	described below under	"Hyperproliferative	Disorders"). Preferred	indications include blood	disorders (e o hynertension
and agonists or antagonists of	the invention) to promote or	inhibit cell proliferation,	activation, and differentiation.	Exemplary assays for ERK	kinase activity that may be	used or routinely modified to	test ERK kinase-induced	activity of polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) include the	assays disclosed in Forrer et	al., Biol Chem 379(8-9):1101-	1110 (1998); Le Marchand-	Brustel Y, Exp Clin	Endocrinol Diabetes	107(2):126-132 (1999);	Kyriakis JM, Biochem Soc	Symp 64:29-48 (1999); Chang	and Karin, Nature	410(6824):37-40 (2001); and	Cobb MH, Prog Biophys Mol	Biol 71(3-4):479-500 (1999);	the contents of each of which	are herein incorporated by	reference in its entirety.	Mouse adipocyte cells that	may be used according to these	assays are publicly available	(P a through the ATCC)
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congestive heart failure, blood	vessel blockage, heart disease,	stroke, impotence and/or as	described below under	"Immune Activity",	"Cardiovascular Disorders",	and/or "Blood-Related	Disorders"), immune disorders	(e.g., as described below under	"Immune Activity"), neural	disorders (e.g., as described	below under "Neural Activity	and Neurological Diseases"),	and infection (e.g., as	described below under	"Infectious Disease").	A highly preferred indication	is diabetes mellitus. An	additional highly preferred	indication is a complication	associated with diabetes (e.g.,	diabetic retinopathy, diabetic	nephropathy, kidney disease	(e.g., renal failure,	nephropathy and/or other	diseases and disorders as	described in the "Renal	Disorders" section below),	diabetic neuropathy, nerve	disease and nerve damage	(e.g., due to diabetic
Exemplary mouse adipocyte	cells that may be used	according to these assays	include 3T3-L1 cells. 3T3-L1	is an adherent mouse	preadipocyte cell line that is a	continuous substrain of 3T3	fibroblast cells developed	through clonal isolation and	undergo a pre-adipocyte to	adipose-like conversion under	appropriate differentiation	conditions known in the art.																		
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		nen	neuropathy), blood vessel
		old	blockage, heart disease, stroke,
		lmi	impotence (e.g., due to diabetic
		ner	neuropathy or blood vessel
		old	blockage), seizures, mental
		cor	confusion, drowsiness,
		lou	nonketotic hyperglycemic-
		hyl	hyperosmolar coma,
		car	cardiovascular disease (e.g.,
		hea	heart disease, atherosclerosis,
	-	mic	microvascular disease,
		hyl	hypertension, stroke, and other
		dis	diseases and disorders as
		des	described in the
		<u>~</u>	"Cardiovascular Disorders"
		oes	section below), dyslipidemia,
		enc	endocrine disorders (as
		sap	described in the "Endocrine
-		Dis	Disorders" section below),
		neu	neuropathy, vision impairment
		(e <sup>8</sup>	(e.g., diabetic retinopathy and
		blii blii	blindness), ulcers and impaired
		ow	wound healing, infection (e.g.,
		linfl	infectious diseases and
		dis	disorders as described in the
		uI"	"Infectious Diseases" section
		bel	below (particularly of the
		urii	urinary tract and skin). An
		adc	additional highly preferred
		bui	indication is obesity and/or
		cor	complications associated with

obesity. Additional highly	preferred indications include	weight loss or alternatively,	weight gain. Additional	highly preferred indications are	complications associated with	insulin resistance.	Additional highly preferred	indications are disorders of the	musculoskeletal systems	including myopathies,	muscular dystrophy, and/or as	described herein.	Additional highly preferred	indications include,	hypertension, coronary artery	disease, dyslipidemia,	gallstones, osteoarthritis,	degenerative arthritis, eating	disorders, fibrosis, cachexia,	and kidney diseases or	disorders. Preferred	indications include neoplasms	and cancer, such as,	Iymphoma, leukemia and	breast, colon, and kidney	cancer. Additional preferred	indications include melanoma,	prostate, lung, pancreatic,	esophageal, stomach, brain,	liver, and urinary cancer.
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					Highly preferred indications include lipomas and liposarcomas. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia.
184	HFABG18	1132	Protection from Endothelial Cell Apoptosis.	Caspase Apoptosis Rescue. Assays for caspase apoptosis rescue are well known in the art and may be used or routinely modified to assess the ability of the polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to inhibit caspase proteasemediated apoptosis. Exemplary assays for caspase apoptosis that may be used or routinely modified to test caspase apoptosis rescue of polypeptides of the invention (including antibodies and agonists or antagonists of the invention include the assays disclosed in Romeo et al	A highly preferred embodiment of the invention includes a method for stimulating endothelial cell growth. An alternative highly preferred embodiment of the invention includes a method for inhibiting endothelial cell growth. A highly preferred embodiment of the invention includes a method for stimulating endothelial cell proliferation. An alternative highly preferred embodiment of the invention includes a method for inhibiting endothelial cell proliferation. A highly preferred embodiment of the invention includes a method for inhibiting embodiment of the invention includes a method for
				Cardiovasc Res 45(3): 788-794 (2000); Messmer et al., Br J Pharmacol 127(7): 1633-1640	stimulating endothelial cell growth. An alternative highly preferred embodiment of the

invention includes a method	for inhibiting endothelial cell	growth. A highly preferred	embodiment of the invention	includes a method for	stimulating apoptosis of	endothelial cells. An	alternative highly preferred	embodiment of the invention	includes a method for	inhibiting (e.g., decreasing)	apoptosis of endothelial cells.	A highly preferred	embodiment of the invention	includes a method for	stimulating angiogenisis. An	alternative highly preferred	embodiment of the invention	includes a method for	inhibiting angiogenesis. A	highly preferred embodiment	of the invention includes a	method for reducing cardiac	hypertrophy. An alternative	highly preferred embodiment	of the invention includes a	method for inducing cardiac	hypertrophy. Highly	preferred indications include	neoplastic diseases (e.g., as	described below under
(1999); and J Atheroscler	Thromb 3(2): 75-80 (1996);	the contents of each of which	are herein incorporated by	reference in its entirety.	Endothelial cells that may be	used according to these assays	are publicly available (e.g.,	through commercial sources).	Exemplary endothelial cells	that may be used according to	these assays include bovine	aortic endothelial cells	(bAEC), which are an example	of endothelial cells which line	blood vessels and are involved	in functions that include, but	are not limited to,	angiogenesis, vascular	permeability, vascular tone,	and immune cell extravasation.										
						*																								

"Hyperproliferative Disorders"), and disorders of	the cardiovascular system	(e.g., heart disease, congestive	heart failure, hypertension,	aortic stenosis,	cardiomyopathy, valvular	regurgitation, left ventricular	dysfunction, atherosclerosis	and atherosclerotic vascular	disease, diabetic nephropathy,	intracardiac shunt, cardiac	hypertrophy, myocardial	infarction, chronic	hemodynamic overload, and/or	as described below under	"Cardiovascular Disorders").	Highly preferred indications	include cardiovascular,	endothelial and/or angiogenic	disorders (e.g., systemic	disorders that affect vessels	such as diabetes mellitus, as	well as diseases of the vessels	themselves, such as of the	arteries, capillaries, veins	and/or lymphatics). Highly	preferred are indications that	stimulate angiogenesis and/or	cardiovascularization. Highly	totionipoi pro productione that

inhibit angiogenesis and/or	cardiovascularization.	Highly preferred indications	include antiangiogenic activity	to treat solid tumors,	leukemias, and Kaposi"s	sarcoma, and retinal disorders.	Highly preferred indications	include neoplasms and cancer,	such as, Kaposi"s sarcoma,	hemangioma (capillary and	cavernous), glomus tumors,	telangiectasia, bacillary	angiomatosis,	hemangioendothelioma,	angiosarcoma,	haemangiopericytoma,	lymphangioma,	lymphangiosarcoma. Highly	preferred indications also	include cancers such as,	prostate, breast, lung, colon,	pancreatic, esophageal,	stomach, brain, liver, and	urinary cancer. Preferred	indications include benign	dysproliferative disorders and	pre-neoplastic conditions, such	as, for example, hyperplasia,	metaplasia, and/or dysplasia.	Highly preferred indications
				,															±								-			

also include arterial disease,	such as, atherosclerosis,	hypertension, coronary artery	disease, inflammatory	vasculitides, Reynaud"s	disease and Reynaud"s	phenomenom, aneurysms,	restenosis; venous and	lymphatic disorders such as	thrombophlebitis,	lymphangitis, and	lymphedema; and other	vascular disorders such as	peripheral vascular disease,	and cancer. Highly	preferred indications also	include trauma such as	wounds, burns, and injured	tissue (e.g., vascular injury	such as, injury resulting from	balloon angioplasty, and	atheroschlerotic lesions),	implant fixation, scarring,	ischemia reperfusion injury,	rheumatoid arthritis,	cerebrovascular disease, renal	diseases such as acute renal	failure, and osteoporosis.	Additional highly preferred	indications include stroke,	graft rejection, diabetic or
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other retinopathies, thrombotic and coagulative disorders.	vascularitis, lymph	angiogenesis, sexual disorders,	age-related macular	degeneration, and treatment	/prevention of endometriosis	and related conditions.	Additional highly preferred	indications include fibromas,	heart disease, cardiac arrest,	heart valve disease, and	vascular disease. Preferred	indications include blood	disorders (e.g., as described	below under "Immune	Activity", "Blood-Related	Disorders", and/or	"Cardiovascular Disorders").	Preferred indications include	autoimmune diseases (e.g.,	rheumatoid arthritis, systemic	lupus erythematosis, multiple	sclerosis and/or as described	below) and	immunodeficiencies (e.g., as	described below). Additional	preferred indications include	inflammation and	inflammatory disorders (such	as acute and chronic
								-														-							
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					inflammatory diseases, e.g., inflammatory bowel disease and Crohn's disease), and pain management.
184	HFABG18	1132	Production of IFNgamma using a T cells	IFNgamma FMAT. IFNg plays a central role in the immune system and is considered to be a proinflammatory cytokine. IFNg promotes TH1 and inhibits TH2 differentiation; promotes IgG2a and inhibits IgE secretion; induces macrophage activation; and increases MHC expression. Assays for immunomodulatory proteins produced by T cells and NK cells that regulate a variety of inflammatory activities and inhibit TH2 helper cell functions are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mediate inflammatory activities, modulate TH2 helper cell function and/or mediate	A highly preferred embodiment of the invention includes a method for stimulating the production of IFNg. An alternative highly preferred embodiment of the invention includes a method for inhibiting the production of IFNg. Highly preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"), and infections, tuberculosis, infections associated with chronic granulomatosus disease and malignant osteoporosis, and/or as described below under "Infectious Disease"). Highly preferred indications include autoimmune disease (e.g., rheumatoid arthritis, systemic lunus erythematosis, multiple

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sclerosis and/or as described	below), immunodeficiency	(e.g., as described below),	boosting a T cell-mediated	immune response, and	suppressing a T cell-mediated	immune response. Additional	highly preferred indications	include inflammation and	inflammatory disorders.	Additional preferred	indications include idiopathic	pulmonary fibrosis. Highly	preferred indications include	neoplastic diseases (e.g.,	leukemia, lymphoma,	melanoma, and/or as described	below under	"Hyperproliferative	Disorders"). Highly preferred	indications include neoplasms	and cancers, such as, for	example, leukemia, lymphoma,	melanoma, and prostate,	breast, lung, colon, pancreatic,	esophageal, stomach, brain,	liver and urinary cancer. Other	preferred indications include	benign dysproliferative	disorders and pre-neoplastic	conditions and for
humoral or cell-mediated	imminity Exemplary assays	that test for	immunomodulatory proteins	evaluate the production of	cytokines, such as Interferon	gamma (IFNg), and the	activation of T cells. Such	assays that may be used or	routinely modified to test	immunomodulatory activity of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include the assays	disclosed in Miraglia et al., J	Biomolecular Screening 4:193-	204 (1999); Rowland et al.,	"Lymphocytes: a practical	approach" Chapter 6:138-160	(2000); Gonzalez et al., J Clin	Lab Anal 8(5):225-233 (1995);	Billiau et al., Ann NY Acad	Sci 856:22-32 (1998); Boehm	et al., Annu Rev Immunol	15:749-795 (1997), and	Rheumatology (Oxford)	38(3):214-20 (1999), the	contents of each of which are	herein incorporated by	
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				Human T cells that may be used according to these assays may be isolated using techniques disclosed herein or otherwise known in the art. Human T cells are primary human lymphocytes that mature in the thymus and express a T Cell receptor and CD3, CD4, or CD8. These cells mediate humoral or cellmediated immunity and may be preactivated to enhance responsiveness to	example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune
	HFABG18	1132	TNFa in Human T-		organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, asthma and allergy.
	HFABG18	1132	SEAP in NK16/STAT6		
 	HFAMB72	1133	Activation of JNK Signaling Pathway in immine cells	Kinase assay. JNK kinase assays for signal transduction that recoulate cell proliferation	Highly preferred indications include asthma, allergy, hypersensitivity reactions.
			(such as eosinophils).	activation, or apoptosis are well known in the art and may	inflammation, and inflammatory disorders.
				be used or routinely modified to assess the ability of	Additional highly preferred indications include immune

a	polypeptides of the invention	and hematopoietic disorders
	(including antibodies and	(e.g., as described below under
<i>√</i> . dd	agonists or antagonists of the	"Immune Activity", and
.11	invention) to promote or	"Blood-Related Disorders"),
II.	inhibit cell proliferation,	autoimmune diseases (e.g.,
2	activation, and apoptosis.	rheumatoid arthritis, systemic
Ш	Exemplary assays for JNK	lupus erythematosis, Crohn"s
N .	kinase activity that may be	disease, multiple sclerosis
n	used or routinely modified to	and/or as described below),
te	test JNK kinase-induced	immunodeficiencies (e.g., as
EZ .	activity of polypeptides of the	described below). Highly
	invention (including antibodies	preferred indications also
8	and agonists or antagonists of	include boosting or inhibiting
# — — — — — — — — — — — — — — — — — — —	the invention) include the	immune cell proliferation.
8	assays disclosed in Forrer et	Preferred indications include
8	al., Biol Chem 379(8-9):1101-	neoplastic diseases (e.g.,
	1110 (1998); Gupta et al., Exp	leukemia, lymphoma, and/or as
	Cell Res 247(2): 495-504	described below under
	(1999); Kyriakis JM, Biochem	"Hyperproliferative
S	Soc Symp 64:29-48 (1999);	Disorders"). Highly preferred
<u> </u>	Chang and Karin, Nature	indications include boosting an
4	410(6824):37-40 (2001); and	eosinophil-mediated immune
<u> </u>	Cobb MH, Prog Biophys Mol	response, and suppressing an
<b>B</b>	Biol 71(3-4):479-500 (1999);	eosinophil-mediated immune
#	the contents of each of which	response.
8	are herein incorporated by	
N	reference in its entirety.	
<u> </u>	Exemplary cells that may be	
	used according to these assays	
	include eosinophils.	
<b>A</b>	Eosinophils are important in	

the late stage of allergic reactions; they are recruited to tissues and mediate the inflammatory response of late stage allergic reaction	Moreover, exemplary assays that may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of	the invention) to modulate signal transduction, cell proliferation, activation, or apoptosis in eosinophils include assays disclosed and/or cited in: Zhang JP, et al., "Role	or caspases in dexamentasone- induced apoptosis and activation of c-Jun NH2- terminal kinase and p38 mitogen-activated protein kinase in human eosinophils" Clin Exp Immunol;	Oct;122(1):20-7 (2000); Hebestreit H, et al., "Disruption of fas receptor signaling by nitric oxide in eosinophils" J Exp Med; Feb 2;187(3):415-25 (1998); J Allergy Clin Immunol 1999
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in in ed (in line). N. In the lits	Assays for the activation of transcription through the Serum Response Element Serum Response Element (SRE) are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to production. Preferred tactors and modulate the serum response factors and modulate the expression of genes involved below under "Immune in growth. Exemplary assays for transcription through the live invention of genes involved below under "Immune in growth. Exemplary assays for transcription through the live invention of genes involved below under "Immune in growth. Exemplary assays for transcription through the live invention of genes involved below under "Immune live in growth. Exemplary assays for transcription through the live invention includes a method for stimulating (e.g., invention) to production. An alternative production. An alternative production. An alternative production. An alternative production includes a method for stimulating (e.g., invention) to production. Preferred embodiment of the invention (including for stimulating (e.g., invention) to production. Preferred embodiment of the invention) to production. Preferred embodiment of the invention) to production. Preferred embodiment of the invention includes a method for stimulating (e.g., invention) to production. Preferred embodiment of the invention includes a method for stimulating (e.g., invention) to production. Preferred embodiment of the invention includes a method for stimulating (e.g., invention) to production. Preferred embodiment of the invention includes a method for stimulating (e.g., invention) to production. Preferred embodiment of the invention includes a method for stimulating (e.g., invention) to production. Preferred embodiment of the invention includes a method for stimulating (e.g., invention) to product in stimulating (e.g., invention) to product in the invention includes a method for stimulating (e.g., invention) to product inven
	transcription through serum response element in (SRE) immune cells (such art and as T-cells). the abil the invariable antiboc antagon regulat factors express in grow for transcription of the contract of the
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	routinely modified to test SRE	Highly preferred indications
	activity of the polypeptides of	include autoimmune diseases
	the invention (including	(e.g., rheumatoid arthritis,
	antibodies and agonists or	systemic lupus erythematosis,
	antagonists of the invention)	Crohn"s disease, multiple
	include assays disclosed in	sclerosis and/or as described
	Berger et al., Gene 66:1-10	below), immunodeficiencies
1-2	(1998); Cullen and Malm,	(e.g., as described below),
	Methods in Enzymol 216:362-	boosting a T cell-mediated
	368 (1992); Henthorn et al.,	immune response, and
	Proc Natl Acad Sci USA	suppressing a T cell-mediated
	85:6342-6346 (1988); and	immune response. Additional
	Black et al., Virus Genes	highly preferred indications
	12(2):105-117 (1997), the	include inflammation and
	content of each of which are	inflammatory disorders, and
	herein incorporated by	treating joint damage in
	reference in its entirety. T	patients with rheumatoid
	cells that may be used	arthritis. An additional highly
	according to these assays are	preferred indication is sepsis.
	publicly available (e.g.,	Highly preferred indications
	through the ATCC).	include neoplastic diseases
	Exemplary mouse T cells that	(e.g., leukemia, lymphoma,
	may be used according to these	and/or as described below
	assays include the CTLL cell	under "Hyperproliferative
	line, which is an IL-2	Disorders"). Additionally,
7.0	dependent suspension culture	highly preferred indications
	of T cells with cytotoxic	include neoplasms and
	activity.	cancers, such as, for example,
		leukemia, lymphoma,
	•	melanoma, glioma (e.g.,
		malignant glioma), solid

tumors, and prostate, breast,	lung, colon, pancreatic,	esophageal, stomach, brain,	liver and urinary cancer. Other	preferred indications include	benign dysproliferative	disorders and pre-neoplastic	conditions, such as, for	example, hyperplasia,	metaplasia, and/or dysplasia.	Preferred indications include	anemia, pancytopenia,	leukopenia, thrombocytopenia,	Hodgkin's disease, acute	lymphocytic anemia (ALL),	plasmacytomas, multiple	myeloma, Burkitt's lymphoma,	arthritis, AIDS, granulomatous	disease, inflammatory bowel	disease, neutropenia,	neutrophilia, psoriasis,	suppression of immune	reactions to transplanted	organs and tissues,	hemophilia, hypercoagulation,	diabetes mellitus, endocarditis,	meningitis, Lyme Disease,	cardiac reperfusion injury, and	asthma and allergy. An	additional preferred indication	is infection (e.g., an infectious
									<del></del>														<del></del>							
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																	<del></del>													

					disease as described below under "Infectious Disease").	
	HFAMH77	1134	Production of IFN gamma using a	IFNgamma FMAT. IFNg plays	A highly preferred	
			T cells	system and is considered to be	embodiment of the invention includes a method for	
				a proinflammatory cytokine.	stimulating the production of	
				IFNg promotes TH1 and	IFNg. An alternative highly	
•				inhibits TH2 differentiation;	preferred embodiment of the	
				promotes IgG2a and inhibits	invention includes a method	
				IgE secretion; induces	for inhibiting the production of	
				macrophage activation; and	IFNg. Highly preferred	
-				increases MHC expression.	indications include blood	
				Assays for immunomodulatory	disorders (e.g., as described	
				proteins produced by T cells	below under "Immune	
				and NK cells that regulate a	Activity", "Blood-Related	
				variety of inflammatory	Disorders", and/or	
				activities and inhibit TH2	"Cardiovascular Disorders"),	
				helper cell functions are well	and infection (e.g., viral	
				known in the art and may be	infections, tuberculosis,	
				used or routinely modified to	infections associated with	
				assess the ability of	chronic granulomatosus	
				polypeptides of the invention	disease and malignant	
				(including antibodies and	osteoporosis, and/or as	
				agonists or antagonists of the	described below under	
		-	i	invention) to mediate	"Infectious Disease"). Highly	
-				immunomodulation, regulate	preferred indications include	
				inflammatory activities,	autoimmune disease (e.g.,	
				modulate TH2 helper cell	rheumatoid arthritis, systemic	
				function, and/or mediate	lupus erythematosis, multiple	
				humoral or cell-mediated	sclerosis and/or as described	
_				immunity. Exemplary assays	below), immunodeficiency	

		that test for	a)	(e.g., as described below),
		immunomodulatory proteins	· -	boosting a T cell-mediated
		evaluate the production of		immune response, and
		cytokines, such as Interferon		suppressing a T cell-mediated
		gamma (IFNg), and the		immune response. Additional
	•	activation of T cells. Such		highly preferred indications
		assays that may be used or		include inflammation and
		routinely modified to test		inflammatory disorders.
		immunomodulatory activity of		Additional preferred
		polypeptides of the invention		indications include idiopathic
		(including antibodies and		pulmonary fibrosis. Highly
		agonists or antagonists of the		preferred indications include
		invention) include the assays		neoplastic diseases (e.g.,
		disclosed in Miraglia et al., J		leukemia, lymphoma,
		Biomolecular Screening 4:193-	93-	melanoma, and/or as described
		204 (1999); Rowland et al.,	<u> </u>	below under
		"Lymphocytes: a practical		"Hyperproliferative
		approach" Chapter 6:138-160		Disorders"). Highly preferred
		(2000); Gonzalez et al., J Clin		indications include neoplasms
		Lab Anal 8(5):225-233 (1995);		and cancers, such as, for
		Billiau et al., Ann NY Acad		example, leukemia, lymphoma,
		Sci 856:22-32 (1998); Boehm		melanoma, and prostate,
		et al., Annu Rev Immunol		breast, lung, colon, pancreatic,
		15:749-795 (1997), and	es	esophageal, stomach, brain,
		Rheumatology (Oxford)		liver and urinary cancer. Other
The state of the s		38(3):214-20 (1999), the		preferred indications include
-		contents of each of which are		benign dysproliferative
		herein incorporated by	<del>Ğ</del>	disorders and pre-neoplastic
		reference in its entirety.	<u>3</u>	conditions, such as, for
		Human T cells that may be		example, hyperplasia,
		used according to these assays		metaplasia, and/or dysplasia.

may be isolated using techniques disclosed herein or techniques disclosed herein or techniques disclosed herein or techniques disclosed herein or therwise known in the art. Human T cells are primary human lymphocytes that human lymphocytes that human lymphocytes that human lymphocytes and CD3, CD4, or CD8. These arthritis, AIDS, granulomatous cells mediated immunity and may be preactivated to enhance immunomodulatory factors. Suppression of immune immunomodulatory factors. Hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, asthma and allergy.	RANTES in immunomodulatory proteins endothelial cells that induce chemotaxis of T (such as human cells, monocytes, and umbilical vein endothelial cells the art and may be used or (HUVEC)) routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mediate immunomodulation, induce chemotaxis and/or
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mediated immunity.  Exemplary assays that test for immunomodulatory proteins evaluate the production of cytokines, such as RANTES, and the induction of chemotactic responses in immune cells. Such assays that may be used or routinely modified to test immunomodulatory activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include the assays disclosed in Miraglia et al., J Biomolecular Screening 4:193-204 (1999); Rowland et al., "Lymphocytes: a practical approach" Chapter 6:138-160 (2000); Cocchi et al., Science 270(5243):1811-1815 (1995); and Robinson et al., Clin Exp Immunol 101(3):398-407 (1995), the contents of each of which are herein incorporated by reference in its entirety. Endothelial cells that may be used according to these assays																															
	mediate humoral or cell-	mediated immunity.	Exemplary assays that test for	immunomodulatory proteins	evaluate the production of	cytokines, such as RANTES,	and the induction of	chemotactic responses in	immune cells. Such assays	that may be used or routinely	modified to test	immunomodulatory activity of	polypeptides of the invention	including antibodies and	agonists or antagonists of the	invention) include the assays	disclosed in Miraglia et al., J	Biomolecular Screening 4:193-	204 (1999); Rowland et al.,	"Lymphocytes: a practical	approach" Chapter 6:138-160	(2000): Cocchi et al., Science	270(5243):1811-1815 (1995);	and Robinson et al., Clin Exp	Immunol 101(3):398-407	(1995), the contents of each of	which are herein incorporated	by reference in its entirety.	Endothelial cells that may be	used according to these assays	are publicly available (e.g.,
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	A highly preferred embodiment of the invention includes a method for inhibiting (e.g., decreasing)  TNF alpha production. An alternative highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing)  TNF alpha production.  Highly preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"), Highly preferred indications include autoimmune diseases
through the ATCC). Exemplary endothelial cells that may be used according to these assays include human umbilical vein endothelial cells (HUVEC), which are endothelial cells which line venous blood vessels, and are involved in functions that include, but are not limited to, angiogenesis, vascular permeability, vascular tone, and immune cell extravasation.	TNFa FMAT. Assays for immunomodulatory proteins produced by activated macrophages, T cells, fibroblasts, smooth muscle, and other cell types that exert a wide variety of inflammatory and cytotoxic effects on a variety of cells are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mediate immunomodulation, modulate inflammation and cytotoxicity. Exemplary
	Production of TNF alpha by dendritic cells
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			assays	assays that test for	(e.g., rheumatoid arthritis,
			immin	immunomodulatory proteins	systemic lupus erythematosis.
			evalua	evaluate the production of	Crohn"s disease, multiple
-			cytokii	cytokines such as tumor	sclerosis and/or as described
			necros	necrosis factor alpha (TNFa),	below), immunodeficiencies
			and the	and the induction or inhibition	(e.g., as described below),
			of an in	of an inflammatory or	boosting a T cell-mediated
	_		cytotox	cytotoxic response. Such	immune response, and
			assays	assays that may be used or	suppressing a T cell-mediated
		_	routine	routinely modified to test	immune response. Additional
			immur	immunomodulatory activity of	highly preferred indications
			polype	polypeptides of the invention	include inflammation and
			(includ	(including antibodies and	inflammatory disorders, and
			agonis	agonists or antagonists of the	treating joint damage in
			inventi	invention) include assays	patients with rheumatoid
		-	disclos	disclosed in Miraglia et al., J	arthritis. An additional highly
			Biomo	Biomolecular Screening 4:193-	preferred indication is sepsis.
	. 4.2	_	204(19	204(1999); Rowland et al.,	Highly preferred indications
			"Lymp	'Lymphocytes: a practical	include neoplastic diseases
			approa	approach" Chapter 6:138-160	(e.g., leukemia, lymphoma,
			(2000)	(2000); Verhasselt et al., Eur J	and/or as described below
			Immur	Immunol 28(11):3886-3890	under "Hyperproliferative
			(1198)	(1198); Dahlen et al., J	Disorders"). Additionally,
	,		Immur	Immunol 160(7):3585-3593	highly preferred indications
	_		(1998)	(1998); Verhasselt et al., J	include neoplasms and
			Immur	Immunol 158:2919-2925	cancers, such as, leukemia,
	_		(1997)	(1997); and Nardelli et al., J	lymphoma, melanoma, glioma
		-	Tenko	Leukoc Biol 65:822-828	(e.g., malignant glioma), solid
			(1999)	(1999), the contents of each of	tumors, and prostate, breast,
			which	which are herein incorporated	lung, colon, pancreatic,
			by refe	by reference in its entirety.	esophageal, stomach, brain,

187	<b>Н</b> FССQ50	1135	Production of IL-4	IL-4 FMAT. Assays for	A highly preferred embodiment of the invention
187	,				embodiment of the invention
				immunomodulatory proteins	
				secreted by TH2 cells that	includes a method for
				stimulate B cells, T cells,	stimulating (e.g., increasing)
				macrophages and mast cells	IL-4 production. An alternative
				and promote polarization of	highly preferred embodiment
				CD4+ cells into TH2 cells are	of the invention includes a
				well known in the art and may	method for inhibiting (e.g.,
				be used or routinely modified	reducing) IL-4 production.
				to assess the ability of	A highly preferred indication
				polypeptides of the invention	includes asthma. A highly
				(including antibodies and	preferred indication includes
				agonists or antagonists of the	allergy. A highly preferred
				invention) to mediate	indication includes rhinitis.
				immunomodulation, stimulate	Additional highly preferred
				immune cells, modulate	indications include
				immune cell polarization,	inflammation and
				and/or mediate humoral or	inflammatory disorders.
				cell-mediated immunity.	Highly preferred indications
				Exemplary assays that test for	include neoplastic diseases
				immunomodulatory proteins	(e.g., leukemia, lymphoma,
				evaluate the production of	melanoma, and/or as described
				cytokines, such as IL-4, and	below under
				the stimulation of immune	"Hyperproliferative
				cells, such as B cells, T cells,	Disorders"). Preferred
-				macrophages and mast cells.	indications include neoplasms
				Such assays that may be used	and cancers, such as, for
				or routinely modified to test	example, leukemia, lymphoma,
-				immunomodulatory activity of	melanoma, and prostate,
				polypeptides of the invention	breast, lung, colon, pancreatic,

							_																			
esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include	benign dysproliferative disorders and pre-neoplastic	conditions, such as, for	example, hyperplasia,	metaplasia, and/or dysplasia.	Preferred indications include	described below under	"Immune Activity", "Blood-	Related Disorders", and/or	"Cardiovascular Disorders").	Preferred indications include	autoimmune diseases (e.g.,	rheumatoid arthritis, systemic	lupus erythematosis, multiple	sclerosis and/or as described	below) and	es (	described below). Preferred	indications include anemia,	pancytopenia, leukopenia,	thrombocytopenia, Hodgkin's	disease, acute lymphocytic	anemia (ALL),	plasmacytomas, multiple	myeloma, Burkitt's lymphoma,	arthritis, AIDS, granulomatous	disease, inflammatory bowel
(including antibodies and agonists or antagonists of the invention) include the assays	disclosed in Miraglia et al., J Biomolecular Screening 4:193-	204 (1999); Rowland et al.,	"Lymphocytes: a practical	approach" Chapter 6:138-160	(2000); Gonzalez et al., J Clin	Lab Anal 8(5):2//-283 (1194);   Vesel et al Res Imminol	144(8):610-616 (1993); Bagley	et al., Nat Immunol 1(3):257-	261 (2000); and van der Graaff	et al., Rheumatology (Oxford)	38(3):214-220 (1999), the	contents of each of which are	herein incorporated by	reference in its entirety.	Human T cells that may be	used according to these assays	may be isolated using	techniques disclosed herein or	otherwise known in the art.	Human T cells are primary	human lymphocytes that	mature in the thymus and	express a T cell receptor and	CD3, CD4, or CD8. These	cells mediate humoral or cell-	mediated immunity and may
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									_		-															

n, tis, se. an ed	S is a second of the second of
disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, and Lyme Disease. An additonal preferred indication is infection (e.g., an infectious disease as described below under "Infectious	Highly preferred indications include inflammatory disorders. Highly preferred indications include immunological and hematopoietic disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"). Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below), and immunodeficiencies (e.g., as described below). An
be preactivated to enhance responsiveness to immunomodulatory factors.	Assays for the activation of transcription through the NFKB response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate NFKB transcription factors and modulate expression of immunomodulatory genes. Exemplary assays for transcription through the NFKB response element that may be used or rountinely modified to test NFKB.
	Activation of transcription through NFKB response element in immune cells (such as the Jurkat human T cell line).
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additional highly preferred indication is infection (e.g., AIDS, and/or an infectious disease as described below	under "Infectious Disease"). Highly preferred indications	(e.g., melanoma, leukemia, lymphoma, and/or as described	"Hyperproliferative "Disorders") Highly preferred	indications include neoplasms	and cancers, such	as,melanoma, renal cell carcinoma, leukemia,	lymphoma, and prostate,	breast, lung, colon, pancreatic,	esopnageal, stomach, brain, liver and urinary cancer. Other	preferred indications include	benign dysproliferative	disorders and pre-neoplastic	conditions, such as, Ior	metaplasia, and/or dysplasia.	Preferred indications also	include anemia, pancytopenia,	leukopenia, thrombocytopenia,	Hodgkin's disease, acute	lymphocytic anemia (ALL),
response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the	invention) include assays disclosed in Berger et al., Gene	Malm, Methods in Enzymol 216:362-368 (1992); Henthorn	85:6342-6346 (1988); Valle Blazonez et al Imminology	90(3):455-460 (1997);	Aramburau et al., J Exp Med	82(3):801-810 (1995); and   Fraser et al., 29(3):838-844	(1999), the contents of each of	which are herein incorporated	cells that may be used	according to these assays are	publicly available (e.g.,	through the ATCC). T cells	that may be used according to	available (e.g., through the	ATCC). Exemplary human T	cells that may be used	according to these assays	include the JURKAT cell line,	which is a suspension culture
			· · · · · · · · · · · · · · · · · · ·							-									_
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	be invention include using invention include using polypeptides of the invention ement (or antibodies, agonists, or antagonists thereof) in detection, diagnosis, prevention, and/or treatment of Inflammation, Infection, tibodies Cancer, Hypersensitivity, and nists of Atherosclerosis.  ate to Atherosclerosis.  ate to of Atherosclerosis.  ate to of Atherosclerosis.
of leukemia cells that produce IL-2 when stimulated.	Assays for the activation of transcription through the Gamma Interferon Activation Site (GAS) response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate STAT transcription factors and modulate gene expression involved in a wide variety of cell functions. Exemplary assays for transcription through the GAS response element that may be used or
	Activation of transcription through GAS response element in immune cells (such as monocytes).
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routinely modified to test	of polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) include assays	disclosed in: Gustafson KS, et	al., J Biol Chem,	271(33):20035-20046 (1996);	Eilers A, et al.,	Immunobiology, 193(2-4):328-	333 (1995); Berger et al., Gene	66:1-10 (1998); Cullen and	Malm, Methods in Enzymol	216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA	85:6342-6346 (1988);	Matikainen et al., Blood	93(6):1980-1991 (1999); and	Henttinen et al., J Immunol	155(10):4582-4587 (1995), the	contents of each of which are	herein incorporated by	reference in its entirety.	Exemplary immune cells that	may be used according to these	assays are publicly available	(e.g., through the ATCC).	Exemplary immune cells that	may be used according to these	assays include the U937 cell
	·-···		<del></del>		,																								

HFCEW05 1136 Production of Assays for VCAM in endothelial cells known in the submitted vein assess the a endothelial cells (HUVEC)) (including agonists or invention) to expression.  HATT may the uppegul (VCAM-1 e endothelial cells are c					line, which is a monocytic cell	
HFCEW05 1136 Production of VCAM in endothelial cells (such as human umbilical vein endothelial cells (HUVEC))					line.	
VCAM in endothelial cells (such as human umbilical vein endothelial cells (HUVEC))		HFCEW05	1136	Production of	Assays for measuring	Highly preferred indications
70. 70	88			VCAM in	expression of VCAM are well-	include inflammation (acute
70				endothelial cells	known in the art and may be	and chronic), restnosis,
				(such as human	used or routinely modified to	atherosclerosis, asthma and
				umbilical vein	assess the ability of	allergy. Highly preferred
				endothelial cells	polypeptides of the invention	indications include
agonists or invention) the workesion.  FMAT may the upregul VCAM-1 e endothelial cells are cells				(HUVEC))	(including antibodies and	inflammation and
invention) t expression. FMAT may the upregul VCAM-1 e endothelial cells are cel vessels, and functions th not limited vascular pe tone, and in extravasatic endothelial used accord include hur endothelial which are a commercial					agonists or antagonists of the	inflammatory disorders,
expression. FMAT may the upregul VCAM-1 e endothelial cells are cel vessels, and functions the not limited vascular perform, and in extravasatic endothelial used accordinclude hum endothelial which are a commercial expression.					invention) to regulate VCAM	immunological disorders,
FMAT may the upregul VCAM-1 e endothelial cells are cel vessels, and functions the not limited vascular pe tone, and in extravasatic endothelial used accordinclude hum endothelial which are a commercial expression					expression. For example,	neoplastic disorders (e.g.
the upregul VCAM-1 e endothelial cells are cel vessels, and functions the not limited vascular pertone, and in extravasatic endothelial used according to the include hun endothelial which are a commercial expression					FMAT may be used to meaure	cancer/tumorigenesis), and
VCAM-1 e endothelial cells are cel vessels, and functions the not limited vascular per tone, and in extravasatic endothelial used accord include hur endothelial which are a commercial expression expression					the upregulation of cell surface	cardiovascular disorders (such
endothelial cells are cel vessels, and functions th not limited vascular pe tone, and in extravasatic endothelial used accord include hur endothelial which are a commercial expression					VCAM-1 expresssion in	as described below under
cells are cel vessels, and functions the not limited vascular per tone, and in extravasatic endothelial used accord include hum endothelial which are a commercial expression expression					endothelial cells. Endothelial	"Immune Activity", "Blood-
vessels, and functions the not limited vascular per tone, and in extravasatic endothelial used according to the include hun endothelial which are a commercial expression	-				cells are cells that line blood	Related Disorders",
functions the not limited vascular per tone, and in extravasatic endothelial used according include hun endothelial which are a commercial expression					vessels, and are involved in	"Hyperproliferative Disorders"
not limited vascular per tone, and in extravasatic endothelial used according include hum endothelial which are a commercial expression expression					functions that include, but are	and/or "Cardiovascular
vascular pe tone, and in extravasatic endothelial used accorc include hur endothelial which are a commercial expression					not limited to, angiogenesis,	Disorders"). Highly preferred
tone, and in extravasatic endothelial used accord include hur endothelial which are a commercial expression					vascular permeability, vascular	indications include neoplasms
extravasati endothelial used accorc include hur endothelial which are a commercial expression					tone, and immune cell	and cancers such as, for
endothelial used accorc include hur endothelial which are a commercial expression					extravasation. Exemplary	example, leukemia, lymphoma,
used accord include hur endothelial which are a commercial expression					endothelial cells that may be	melanoma, renal cell
include hur endothelial which are a commercial expression					used according to these assays	carcinoma, and prostate,
endothelial which are a commercial expression					include human umbilical vein	breast, lung, colon, pancreatic,
which are a commercial expression					endothelial cells (HUVEC),	esophageal, stomach, brain,
commercial					which are available from	liver and urinary cancer. Other
expression					commercial sources. The	preferred indications include
					expression of VCAM	benign dysproliferative
(CD106), a			And the second s		(CD106), a membrane-	disorders and pre-neoplastic

conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia.			A highly preferred indication is diabetes mellitus.	Additional highly preterred indications include	complications associated with diabetes (e.g., diabetic	retinopathy, diabetic	nephropatny, kidney disease (e.g., renal failure,	nephropathy and/or other	diseases and disorders as described in the "Renal	Disorders" section below),	diabetic neuropathy, nerve	disease and nerve damage	(e.g., due to diabetic
associated protein, can be upregulated by cytokines or other factors, and contributes to the extravasation of lymphocytes, leucocytes and other immune cells from blood vessels; thus VCAM expression plays a role in promoting immune and inflammatory responses.			Assays for the regulation of transcription through the	DMEFI response element are well-known in the art and may	be used or routinely modified to assess the ability of	polypeptides of the invention	(including antibodies and agonists or antagonists of the	invention) to activate the	DMEF1 response element in a reporter construct (such as that	containing the GLUT4	promoter) and to regulate	insulin production. The	DMEF1 response element is
	SEAP in Jurkat/IL4 promoter (antiCD3 co-stim)	SEAP in Senescence Assay	Regulation of transcription via	DMEF1 response element in	adipocytes and pre-	•							
	1136	1136	1137	·									
	HFCEW05	HFCEW05	HFFAD59										
	188	188	189										

	present in the GLITT4	neuropathy), blood vessel
	promoter and binds to MEF2	blockage, heart disease, stroke,
	transcription factor and another	impotence (e.g., due to diabetic
	transcription factor that is	neuropathy or blood vessel
	required for insulin regulation	blockage), seizures, mental
	of Glut4 expression in skeletal	confusion, drowsiness,
	muscle. GLUT4 is the primary	nonketotic hyperglycemic-
	insulin-responsive glucose	hyperosmolar coma,
	transporter in fat and muscle	cardiovascular disease (e.g.,
	tissue. Exemplary assays that	heart disease, atherosclerosis,
	may be used or routinely	microvascular disease,
	modified to test for DMEF1	hypertension, stroke, and other
	response element activity (in	diseases and disorders as
	adipocytes and pre-adipocytes)	described in the
	by polypeptides of the	"Cardiovascular Disorders"
	invention (including antibodies	section below), dyslipidemia,
	and agonists or antagonists of	endocrine disorders (as
	the invention) include assays	described in the "Endocrine
	disclosed inThai, M.V., et al., J	Disorders" section below),
	Biol Chem, 273(23):14285-92	neuropathy, vision impairment
	(1998); Mora, S., et al., J Biol	(e.g., diabetic retinopathy and
	Chem, 275(21):16323-8	blindness), ulcers and impaired
	(2000); Liu, M.L., et al., J Biol	wound healing, and infection
	Chem, 269(45):28514-21	(e.g., infectious diseases and
	(1994); "Identification of a 30-	disorders as described in the
 -	base pair regulatory element	"Infectious Diseases" section
	and novel DNA binding	below, especially of the
	protein that regulates the	urinary tract and skin). An
	human GLUT4 promoter in	additional highly preferred
	transgenic mice", J Biol Chem.	indication is obesity and/or
	2000 Aug 4;275(31):23666-73;	complications associated with

Berger, et al., Gene 66:1-10 obesity. Additional highly (1988); and, Cullen, B., et al., Mefende in Fraymol	the nich is		Adipocytes and pre-adipocytes that may be used according to	these assays are publicly	available (e.g., through the	ATCC) and/or may be	routinely generated.	Exemplary cells that may be	used according to these assays	include the mouse 2T2. I feel	TICATOR OF THE TICATO	line which is an adherent	line which is an adherent mouse preadipocyte cell line.	line which is an adherent mouse preadipocyte cell line.  Mouse 3T3-L1 cells are a	line which is an adherent mouse preadipocyte cell line. Mouse 3T3-L1 cells are a continuous substrain of 3T3	line which is an adherent mouse preadipocyte cell line. Mouse 3T3-L1 cells are a continuous substrain of 3T3 fibroblasts developed through	line which is an adherent mouse preadipocyte cell line. Mouse 3T3-L1 cells are a continuous substrain of 3T3 fibroblasts developed through clonal isolation. These cells	line which is an adherent mouse preadipocyte cell line. Mouse 3T3-L1 cells are a continuous substrain of 3T3 fibroblasts developed through clonal isolation. These cells undergo a pre-adipocyte to	line which is an adherent mouse preadipocyte cell line. Mouse 3T3-L1 cells are a continuous substrain of 3T3 fibroblasts developed through clonal isolation. These cells undergo a pre-adipocyte to adipose-like conversion under	line which is an adherent mouse preadipocyte cell line. Mouse 3T3-L1 cells are a continuous substrain of 3T3 fibroblasts developed through clonal isolation. These cells undergo a pre-adipocyte to adipose-like conversion under	line which is an adherent mouse preadipocyte cell line. Mouse 3T3-L1 cells are a continuous substrain of 3T3 fibroblasts developed through clonal isolation. These cells undergo a pre-adipocyte to adipose-like conversion under appropriate differentiation culture conditions.	line which is an adherent mouse preadipocyte cell line. Mouse 3T3-L1 cells are a continuous substrain of 3T3 fibroblasts developed through clonal isolation. These cells undergo a pre-adipocyte to adipose-like conversion under appropriate differentiation culture conditions.  Activation of Assays for the activation of Preferred indications	line which is an adherent mouse preadipocyte cell line. Mouse 3T3-L1 cells are a continuous substrain of 3T3 fibroblasts developed through clonal isolation. These cells undergo a pre-adipocyte to adipose-like conversion under appropriate differentiation culture conditions.  Activation of transcription transcription transcription through the AP1	line which is an adherent mouse preadipocyte cell line. Mouse 3T3-L1 cells are a continuous substrain of 3T3 fibroblasts developed through clonal isolation. These cells undergo a pre-adipocyte to adipose-like conversion under appropriate differentiation culture conditions.  Activation of transcription through AP1 response element are known in
(1988) Metho	216:30 conter	herein refere	Adipo that m	these	availa	ATCC	routin	Exem	used a			Includ Includ	line w mouse	line w mouse mouse Mouse	includ line w mouse Mouse Mouse contin	includ includ line w includ includ includ include with including i	Ine w mouse Mouse Contine tibrob clonal	Includ Includ Includ Includ Includ Includ Includ Include Including	Includ line w mouse Mouse Mouse contin fibrob clonal under adipos	line w Innouse Mouse Contin fibrob clonal under; adipos	line w mouse Mouse Contin fibrob clonal under appro		£	د_
																						1137	1137	1137
																						HFFAD59	HFFAD59	HFFAD59
											-		<b>37</b> 4 - 1879								7. 7. 7. 7. 7. 7. 7. 7. 7. 7. 7. 7. 7. 7			

	as T-cells).	the ability of polypeptides of	(e.g., as described below under
		the invention (including	"Immune Activity",
		antibodies and agonists or	"Cardiovascular Disorders",
		antagonists of the invention) to	and/or "Blood-Related
		modulate growth and other cell	Disorders"), and infection
		functions. Exemplary assays	(e.g., an infectious disease as
		for transcription through the	described below under
		AP1 response element that	"Infectious Disease"). Highly
		may be used or routinely	preferred indications include
		modified to test AP1-response	autoimmune diseases (e.g.,
		element activity of	rheumatoid arthritis, systemic
		polypeptides of the invention	lupus erythematosis, multiple
		(including antibodies and	sclerosis and/or as described
		agonists or antagonists of the	below) and
<del></del>		invention) include assays	immunodeficiencies (e.g., as
	•	disclosed in Berger et al., Gene	described below). Additional
		66:1-10 (1988); Cullen and	highly preferred indications
		Malm, Methods in Enzymol	include inflammation and
		216:362-368 (1992); Henthorn	inflammatory disorders.
		et al., Proc Natl Acad Sci USA	Highly preferred indications
		85:6342-6346 (1988);	also include neoplastic
		Rellahan et al., J Biol Chem	diseases (e.g., leukemia,
	-	272(49):30806-30811 (1997);	lymphoma, and/or as described
		Chang et al., Mol Cell Biol	below under
		18(9):4986-4993 (1998); and	"Hyperproliferative
		Fraser et al., Eur J Immunol	Disorders"). Highly preferred
		29(3):838-844 (1999), the	indications include neoplasms
		contents of each of which are	and cancers, such as, leukemia,
		herein incorporated by	lymphoma, prostate, breast,
		reference in its entirety. T	lung, colon, pancreatic,
10.100		cells that may be used	esophageal, stomach, brain,

			according to these assays are publicly available (e.g., through the ATCC).	liver, and urinary cancer. Other preferred indications include benign dysproliferative
	<u> </u>		Exemplary mouse 1 cells that may be used according to these assays include the CTLL cell	disorders and pre-neoplastic conditions, such as, for example, hyperplasia,
			line, which is an IL-2	metaplasia, and/or dysplasia.
			dependent suspension-cuiture cell line with cytotoxic	arthritis, asthma, AIDS,
7 4-44			activity.	allergy, anemia, pancytopenia,
	***			Hodgkin's disease, acute
				lymphocytic anemia (ALL),
				plasmacytomas, multiple
				myeloma, Burkitt's lymphoma,
				granulomatous disease,
				inflammatory bowel disease,
				sepsis, psoriasis, suppression
				of immune reactions to
		•		transplanted organs and
				tissues, endocarditis,
				meningitis, and Lyme Disease.
HFFAD59	1137	Activation of	Assays for the activation of	A preferred embodiment of
		transcription	transcription through the	the invention includes a
		through serum	Serum Response Element	method for inhibiting (e.g.,
		response element in	(SRE) are well-known in the	reducing) TNF alpha
		immune cells (such	art and may be used or	production. An alternative
		as T-cells).	routinely modified to assess	preferred embodiment of the
			the ability of polypeptides of	invention includes a method
-			the invention (including	for stimulating (e.g.,
			antibodies and agonists or	increasing) TNF alpha

															-														
production. Preferred indications include blood	disorders (e.g., as described	below under "Immune	Activity", "Blood-Related	Disorders", and/or	"Cardiovascular Disorders"),	Highly preferred indications	include autoimmune diseases	(e.g., rheumatoid arthritis,	systemic lupus erythematosis,	Crohn"s disease, multiple	sclerosis and/or as described	below), immunodeficiencies	(e.g., as described below),	boosting a T cell-mediated	immune response, and	suppressing a T cell-mediated	immune response. Additional	highly preferred indications	include inflammation and	inflammatory disorders, and	treating joint damage in	patients with rheumatoid	arthritis. An additional highly	preferred indication is sepsis.	Highly preferred indications	include neoplastic diseases	(e.g., leukemia, lymphoma,	and/or as described below	under "Hyperproliferative
antagonists of the invention) to	factors and modulate the	expression of genes involved	in growth. Exemplary assays	for transcription through the	SRE that may be used or	routinely modified to test SRE	activity of the polypeptides of	the invention (including	antibodies and agonists or	antagonists of the invention)	include assays disclosed in	Berger et al., Gene 66:1-10	(1998); Cullen and Malm,	Methods in Enzymol 216:362-	368 (1992); Henthorn et al.,	Proc Natl Acad Sci USA	85:6342-6346 (1988); and	Black et al., Virus Genes	12(2):105-117 (1997), the	content of each of which are	herein incorporated by	reference in its entirety. T	cells that may be used	according to these assays are	publicly available (e.g.,	through the ATCC).	Exemplary mouse T cells that	may be used according to these	assays include the CTLL cell
			-																										
											_																		

Disorders"). Additionally, highly preferred indications include neoplasms and cancers such as for example.	leukemia, lymphoma, melanoma, glioma (e.g., malignant glioma), solid tumors, and prostate, breast,	lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include	benign dysproliferative disorders and pre-neoplastic conditions, such as, for	example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include	anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL),	plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous	disease, inflammatory bowel disease, neutropenia, neutrophilia, psoriasis,	suppression of immune reactions to transplanted organs and tissues,
line, which is an IL-2 dependent suspension culture of T cells with cytotoxic	activity.							

	,				hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, cardiac reperfusion injury, and asthma and allergy. An additional preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease").
189	HFFAD59	1137	SEAP in Senescence Assay		
190	HFFAL36	1138	Activation of transcription through AP1 response element in immune cells (such as T-cells).	Assays for the activation of transcription through the AP1 response element are known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to modulate growth and other cell functions. Exemplary assays for transcription through the AP1 response element that may be used or routinely modified to test AP1-response element activity of polypeptides of the invention (including antibodies and	Preferred indications include neoplastic diseases (e.g., as described below under "Hyperproliferative Disorders"), blood disorders (e.g., as described below under "Immune Activity", "Cardiovascular Disorders", and/or "Blood-Related Disorders"), and infection (e.g., an infectious disease as described below under "Infectious Disease"). Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described
				agonists or antagonists of the invention) include assays	below) and immunodeficiencies (e.g., as

		disclosed in Berger et al., Gene	described below). Additional
		66:1-10 (1988); Cullen and	highly preferred indications
	_	Malm, Methods in Enzymol	include inflammation and
		216:362-368 (1992); Henthorn	inflammatory disorders.
		et al., Proc Natl Acad Sci USA	Highly preferred indications
		85:6342-6346 (1988);	also include neoplastic
-		Rellahan et al., J Biol Chem	diseases (e.g., leukemia,
		272(49):30806-30811 (1997);	lymphoma, and/or as described
		Chang et al., Mol Cell Biol	below under
		18(9):4986-4993 (1998); and	"Hyperproliferative
		Fraser et al., Eur J Immunol	Disorders"). Highly preferred
		29(3):838-844 (1999), the	indications include neoplasms
		contents of each of which are	and cancers, such as, leukemia,
		herein incorporated by	lymphoma, prostate, breast,
		reference in its entirety. T	lung, colon, pancreatic,
		cells that may be used	esophageal, stomach, brain,
		according to these assays are	liver, and urinary cancer. Other
		publicly available (e.g.,	preferred indications include
		through the ATCC).	benign dysproliferative
		Exemplary mouse T cells that	disorders and pre-neoplastic
		may be used according to these	conditions, such as, for
		assays include the CTLL cell	example, hyperplasia,
		line, which is an IL-2	metaplasia, and/or dysplasia.
		dependent suspension-culture	Preferred indications include
		cell line with cytotoxic	arthritis, asthma, AIDS,
		activity.	allergy, anemia, pancytopenia,
			leukopenia, thrombocytopenia,
	_		Hodgkin's disease, acute
			lymphocytic anemia (ALL),
			plasmacytomas, multiple
			myeloma, Burkitt's lymphoma,

					granulomatous disease,
-					inflammatory bowel disease,
					sepsis, psoriasis, suppression
					of immune reactions to
					transplanted organs and
	-				tissues, endocarditis,
ļ					meningitis, and Lyme Disease.
	HFFAL36	1138	Activation of	Assays for the activation of	A preferred embodiment of
190			transcription	transcription through the	the invention includes a
			through serum	Serum Response Element	method for inhibiting (e.g.,
			response element in	(SRE) are well-known in the	reducing) TNF alpha
			immune cells (such	art and may be used or	production. An alternative
			as T-cells).	routinely modified to assess	preferred embodiment of the
				the ability of polypeptides of	invention includes a method
	-			the invention (including	for stimulating (e.g.,
				antibodies and agonists or	increasing) TNF alpha
				antagonists of the invention) to	production. Preferred
				regulate the serum response	indications include blood
				factors and modulate the	disorders (e.g., as described
				expression of genes involved	below under "Immune
				in growth. Exemplary assays	Activity", "Blood-Related
				for transcription through the	Disorders", and/or
				SRE that may be used or	"Cardiovascular Disorders"),
				routinely modified to test SRE	Highly preferred indications
-				activity of the polypeptides of	include autoimmune diseases
				the invention (including	(e.g., rheumatoid arthritis,
				antibodies and agonists or	systemic lupus erythematosis,
				antagonists of the invention)	Crohn"s disease, multiple
				include assays disclosed in	sclerosis and/or as described
				Berger et al., Gene 66:1-10	below), immunodeficiencies
				(1998); Cullen and Malm,	(e.g., as described below),

Methods in Enzymol 216:362- 368 (1992); Henthom et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); and Black et al., Virus Genes 12(2):105-117 (1997), the content of each of which are herein incorporated by reference in its entirety. T cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary mouse T cells that may be used according to these assays include the CTLL cell line, which is an IL-2 dependent suspension culture of T cells with cytotoxic activity.	:362- boosting a T cell-mediated immune response, and suppressing a T cell-mediated	d immune response. Additional highly preferred indications include inflammation and		T patients with rheumatoid arthritis. An additional highly	are preferred indication is sepsis. Highly preferred indications	include neoplastic diseases		these and/or as described below cell under "Hyperproliferative			include neoplasms and	cancers, such as, for example, leukemia. Ivmphoma.	melanoma, glioma (e.g.,	malignant glioma), solid	tumors, and prostate, breast,	lung, colon, pancreatic,	esophageal, stomach, brain,	liver and urinary cancer. Other	preferred indications include	benign dysproliferative	disorders and pre-neoplastic	conditions, such as, for
	Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA	85:6342-6346 (1988); and Black et al., Virus Genes 12(2):105-117 (1997). the	content of each of which are herein incorporated by	reference in its entirety. T cells that may be used	according to these assays are publicly available (e.g.,	through the ATCC).	Exemplary mouse T cells that	may be used according to assays include the CTLL	line, which is an IL-2	dependent suspension culture	of T cells with cytotoxic	activity.										

L36 1138 IL-10 in Human T- cell 2B9 AD82 1139 SEAP in HepG2/Squale- synthetase(stimulati	example, nyperplasta, metaplasia, and/or dysplasia. Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, inflammatory bowel disease, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, cardiac reperfusion injury, and asthma and allergy. An additional preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease").		
		IL-10 in Human T-cell 2B9	SEAP in HepG2/Squale- synthetase(stimulati
<b>√</b>   <b>₹</b>		HFFAL36   1138	HFGAD82 1139

191	HFGAD82	1139	SEAP in HIB/CRE		
	HFGAD82	1139	Activation of	Assays for the activation of	Preferred indications
191			transcription	transcription through the AP1	include neoplastic diseases
			through AP1	response element are known in	(e.g., as described below under
			response element in	the art and may be used or	"Hyperproliferative
			immune cells (such	routinely modified to assess	Disorders"), blood disorders
			as T-cells).	the ability of polypeptides of	(e.g., as described below under
				the invention (including	"Immune Activity",
				antibodies and agonists or	"Cardiovascular Disorders",
				antagonists of the invention) to	and/or "Blood-Related
				modulate growth and other cell	Disorders"), and infection
	-	-		functions. Exemplary assays	(e.g., an infectious disease as
		- e.		for transcription through the	described below under
				AP1 response element that	"Infectious Disease"). Highly
				may be used or routinely	preferred indications include
				modified to test AP1-response	autoimmune diseases (e.g.,
				element activity of	rheumatoid arthritis, systemic
				polypeptides of the invention	lupus erythematosis, multiple
				(including antibodies and	sclerosis and/or as described
				agonists or antagonists of the	below) and
				invention) include assays	immunodeficiencies (e.g., as
1-0				disclosed in Berger et al., Gene	described below). Additional
				66:1-10 (1988); Cullen and	highly preferred indications
				Malm, Methods in Enzymol	include inflammation and
				216:362-368 (1992); Henthorn	inflammatory disorders.
				et al., Proc Natl Acad Sci USA	Highly preferred indications
				85:6342-6346 (1988);	also include neoplastic
				Rellahan et al., J Biol Chem	diseases (e.g., leukemia,
				272(49):30806-30811 (1997);	lymphoma, and/or as described
,				Chang et al., Mol Cell Biol	below under

				<u> </u>	Discussion Uighly professed
				Fraser et al., Eur J Immunol 29(3):838-844 (1999), the	indications include neoplasms
				contents of each of which are	and cancers, such as, leukemia,
				herein incorporated by	lymphoma, prostate, breast,
				reference in its entirety.	lung, colon, pancreatic,
				Mouse T cells that may be	esophageal, stomach, brain,
				used according to these assays	liver, and urinary cancer. Other
				are publicly available (e.g.,	preferred indications include
				through the ATCC).	benign dysproliferative
				Exemplary mouse T cells that	disorders and pre-neoplastic
				may be used according to these	conditions, such as, for
				assays include the HT2 cell	example, hyperplasia,
				line, which is an IL-2	metaplasia, and/or dysplasia.
				dependent suspension culture	Preferred indications include
				cell line that also responds to	arthritis, asthma, AIDS,
				IL-4.	allergy, anemia, pancytopenia,
					leukopenia, thrombocytopenia,
					Hodgkin's disease, acute
					lymphocytic anemia (ALL),
					plasmacytomas, multiple
					myeloma, Burkitt's lymphoma,
					granulomatous disease,
_		-			inflammatory bowel disease,
					sepsis, psoriasis, suppression
-					of immune reactions to
					transplanted organs and
					tissues, endocarditis,
					meningitis, and Lyme Disease.
	HFGAD82	1139	Stimulation of	Assays for measuring secretion	A highly preferred
•		·  -  -	insulin secretion	of insulin are well-known in	indication is diabetes mellitus.

	from pancreatic	the art and may be used or	An additional highly preferred
	beta cells.	routinely modified to assess	indication is a complication
-		the ability of polypeptides of	associated with diabetes (e.g.,
		the invention (including	diabetic retinopathy, diabetic
		antibodies and agonists or	nephropathy, kidney disease
		antagonists of the invention) to	(e.g., renal failure,
		stimulate insulin secretion.	nephropathy and/or other
-		For example, insulin secretion	diseases and disorders as
		is measured by FMAT using	described in the "Renal
		anti-rat insulin antibodies.	Disorders" section below),
		Insulin secretion from	diabetic neuropathy, nerve
		pancreatic beta cells is	disease and nerve damage
		upregulated by glucose and	(e.g., due to diabetic
		also by certain	neuropathy), blood vessel
		proteins/peptides, and	blockage, heart disease, stroke,
		disregulation is a key	impotence (e.g., due to diabetic
	-	component in diabetes.	neuropathy or blood vessel
		Exemplary assays that may be	blockage), seizures, mental
		used or routinely modified to	confusion, drowsiness,
		test for stimulation of insulin	nonketotic hyperglycemic-
		secretion (from pancreatic	hyperosmolar coma,
		cells) by polypeptides of the	cardiovascular disease (e.g.,
		invention (including antibodies	heart disease, atherosclerosis,
		and agonists or antagonists of	microvascular disease,
		the invention) include assays	hypertension, stroke, and other
		disclosed in: Ahren, B., et al.,	diseases and disorders as
		Am J Physiol, 277(4 Pt	described in the
		2):R959-66 (1999); Li, M., et	"Cardiovascular Disorders"
		al., Endocrinology,	section below), dyslipidemia,
		138(9):3735-40 (1997); Kim,	endocrine disorders (as
		K.H., et al., FEBS Lett,	described in the "Endocrine

				377(2):237-9 (1995); and,	Disorders" section below),
			,-	Miraglia S et. al., Journal of	neuropathy, vision impairment
	Y			Biomolecular Screening,	(e.g., diabetic retinopathy and
	_			4:193-204 (1999), the contents	blindness), ulcers and impaired
				of each of which is herein	wound healing, and infection
				incorporated by reference in its	(e.g., infectious diseases and
				entirety. Pancreatic cells that	disorders as described in the
				may be used according to these	"Infectious Diseases" section
				assays are publicly available	below, especially of the
				(e.g., through the ATCC)	urinary tract and skin), carpal
				and/or may be routinely	tunnel syndrome and
				generated. Exemplary	Dupuytren's contracture).
				pancreatic cells that may be	An additional highly preferred
				used according to these assays	indication is obesity and/or
				include rat INS-1 cells. INS-1	complications associated with
				cells are a semi-adherent cell	obesity. Additional highly
				line established from cells	preferred indications include
				isolated from an X-ray induced	weight loss or alternatively,
				rat transplantable insulinoma.	weight gain. Aditional
				These cells retain	highly preferred indications are
				characteristics typical of native	complications associated with
				pancreatic beta cells including	insulin resistance.
				glucose inducible insulin	
				secretion. References: Asfari	
				et al. Endocrinology 1992	
				130:167.	
	HFIIZ70	1140	Activation of JNK	Kinase assay. JNK kinase	Highly preferred indications
92			Signaling Pathway	assays for signal transduction	include asthma, allergy,
			in immune cells	that regulate cell proliferation,	hypersensitivity reactions,
			(such as	activation, or apoptosis are	inflammation, and
			eosinophils).	well known in the art and may	inflammatory disorders.

Additional highly preferred	indications include immune	and hematopoietic disorders	(e.g., as described below under	"Immune Activity", and	"Blood-Related Disorders"),	autoimmune diseases (e.g.,	rheumatoid arthritis, systemic	lupus erythematosis, Crohn"s	disease, multiple sclerosis	and/or as described below),	immunodeficiencies (e.g., as	described below). Highly	preferred indications also	include boosting or inhibiting	immune cell proliferation.	Preferred indications include	neoplastic diseases (e.g.,	leukemia, lymphoma, and/or as	described below under	"Hyperproliferative	Disorders"). Highly preferred	indications include boosting an	eosinophil-mediated immune	response, and suppressing an	eosinophil-mediated immune	response.				
be used or routinely modified	to assess the ability of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) to promote or	inhibit cell proliferation,	activation, and apoptosis.	Exemplary assays for JNK	kinase activity that may be	used or routinely modified to	test JNK kinase-induced	activity of polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) include the	assays disclosed in Forrer et	al., Biol Chem 379(8-9):1101-	1110 (1998); Gupta et al., Exp	Cell Res 247(2): 495-504	(1999); Kyriakis JM, Biochem	Soc Symp 64:29-48 (1999);	Chang and Karin, Nature	410(6824):37-40 (2001); and	Cobb MH, Prog Biophys Mol	Biol 71(3-4):479-500 (1999);	the contents of each of which	are herein incorporated by	reference in its entirety.	Exemplary cells that may be	used according to these assays
																										-				

include eosinophils.  Eosinophils are important in the late stage of allergic reactions; they are recruited to tissues and mediate the	inflammatory response of late stage allergic reaction.  Moreover, exemplary assays that may be used or routinely modified to assess the ability of polypeptides of the	and agonists or antagonists of the invention) to modulate signal transduction, cell proliferation, activation, or apoptosis in eosinophils include assays disclosed and/or	of caspases in dexamethasone- induced apoptosis and activation of c-Jun NH2- terminal kinase and p38 mitogen-activated protein	Clin Exp Immunol; Oct;122(1):20-7 (2000); Hebestreit H, et al., "Disruption of fas receptor signaling by nitric oxide in eosinophils" J Exp Med; Feb

2;187(3):415-25 (1998); J Allergy Clin Immunol 1999 Sep;104(3 Pt 1):565-74; and, Sousa AR, et al., "In vivo resistance to corticosteroids in bronchial asthma is associated with enhanced phosyphorylation of JUN N- terminal kinase and failure of prednisolone to inhibit JUN N- terminal kinase phosphorylation" J Allergy Clin Immunol; Sep;104(3 Pt 1):565-74 (1999); the contents of each of which are herein incorporated by reference in its entirety.	Caspase Apoptosis. Assays for caspase apoptosis are well known in the art and may be used or routinely modified to assess the ability of assess the ability of polypeptides of the invention polypeptides of the invention polypeptides of the invention polypeptides of the invention detection, diagnosis, prevention, and/or treatment of asthma, allergy, invention) to regulate caspase protease-mediated apoptosis in inflammation.  Treated embodiments of the invention or antagonists or antagonists of the invention detection, diagnosis, prevention, and/or treatment of asthma, allergy, inflammation.  Inflammation.  Treated embodiments of the invention or antagonists or antagonists of the invention detection, diagnosis, prevention, and/or treatment of asthma, allergy, inflammation.  Inflammation.
2;187(3):415-25 Allergy Clin Im Sep;104(3 Pt 1) Sousa AR, et all resistance to con bronchial asthm with enhanced phosyphorylatic terminal kinase prednisolone to terminal kinase phosphorylatior Clin Immunol; 3 1):565-74 (1999) of each of whicl incorporated by entirety.	Regulation of caspase Apoptosis. caspase apoptosis ar immune cells (such as mast cells).  as mast cells).  assess the ability of polypeptides of the infinction invention invention to regulate protease-mediated a immune cells (such example, in mast cells are found in column and mucosal tissues
	HFKET18 1141
	H 193

the body, and their activation	via immunoglobulin E -	antigen, promoted by T helper	cell type 2 cytokines, is an	important component of	allergic disease. Dysregulation	of mast cell apoptosis may	play a role in allergic disease	and mast cell tumor survival.	Exemplary assays for caspase	apoptosis that may be used or	routinely modified to test	capase apoptosis activity	induced by polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) include the	assays disclosed in: Masuda A,	et al., J Biol Chem,	276(28):26107-26113 (2001);	Yeatman CF 2nd, et al., J Exp	Med, 192(8):1093-1103	(2000);Lee et al., FEBS Lett	485(2-3): 122-126 (2000); Nor	et al., J Vasc Res 37(3): 209-	218 (2000); and Karsan and	Harlan, J Atheroscler Thromb	3(2): 75-80 (1996); the	contents of each of which are	herein incorporated by	reference in its entirety.
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				Immune cells that may be used	
				according to these assays are	
				publicly available (e.g.,	
				through commercial sources).	
				Exemplary immune cells that	
	×=-			may be used according to these	
				assays include mast cells such	
				as the HMC human mast cell	
				line.	
	HFKET18	1141	Activation of	Assays for the activation of	Highly preferred indications
193			transcription	transcription through the	include blood disorders (e.g.,
			through NFAT	Nuclear Factor of Activated T	as described below under
			response in immune	cells (NFAT) response element	"Immune Activity", "Blood-
			cells (such as T-	are well-known in the art and	Related Disorders", and/or
			cells).	may be used or routinely	"Cardiovascular Disorders").
,				modified to assess the ability	Highly preferred indications
				of polypeptides of the	include autoimmune diseases
				invention (including antibodies	(e.g., rheumatoid arthritis,
	-419		-	and agonists or antagonists of	systemic lupus erythematosis,
				the invention) to regulate	multiple sclerosis and/or as
				NFAT transcription factors and	described below),
				modulate expression of genes	immunodeficiencies (e.g., as
				involved in	described below), boosting a T
				immunomodulatory functions.	cell-mediated immune
				Exemplary assays for	response, and suppressing a T
				transcription through the	cell-mediated immune
				NFAT response element that	response. Additional highly
				may be used or routinely	preferred indications include
· ·				modified to test NFAT-	inflammation and
				response element activity of	inflammatory disorders. An
				polypeptides of the invention	additional highly preferred

		(including antibodies and	indication is infection (e.g., an
		agonists or antagonists of the	infectious disease as described
		invention) include assays	below under "Infectious
		disclosed in Berger et al., Gene	Disease"). Preferred
		66:1-10 (1998); Cullen and	indications include neoplastic
		Malm, Methods in Enzymol	diseases (e.g., leukemia,
	-	216:362-368 (1992); Henthorn	lymphoma, and/or as described
		et al., Proc Natl Acad Sci USA	below under
		85:6342-6346 (1988); Serfling	"Hyperproliferative
		et al., Biochim Biophys Acta	Disorders"). Preferred
		1498(1):1-18 (2000); De Boer	indications include neoplasms
		et al., Int J Biochem Cell Biol	and cancers, such as, for
		31(10):1221-1236 (1999);	example, leukemia, lymphoma,
`		Fraser et al., Eur J Immunol	and prostate, breast, lung,
		29(3):838-844 (1999); and	colon, pancreatic, esophageal,
		Yeseen et al., J Biol Chem	stomach, brain, liver and
		268(19):14285-14293 (1993),	urinary cancer. Other preferred
		the contents of each of which	indications include benign
		are herein incorporated by	dysproliferative disorders and
		reference in its entirety. T	pre-neoplastic conditions, such
		cells that may be used	as, for example, hyperplasia,
		according to these assays are	metaplasia, and/or dysplasia.
		publicly available (e.g.,	Preferred indications also
		through the ATCC).	include anemia, pancytopenia,
		Exemplary human T cells that	leukopenia, thrombocytopenia,
		may be used according to these	Hodgkin's disease, acute
		assays include the JURKAT	lymphocytic anemia (ALL),
		cell line, which is a suspension	plasmacytomas, multiple
		culture of leukemia cells that	myeloma, Burkitt's lymphoma,
		produce IL-2 when stimulated.	arthritis, AIDS, granulomatous
-			disease, inflammatory bowel

disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, asthma and allergy.	A highly preferred embodiment of the invention includes a method for stimulating natural killer cell proliferation. An alternative highly preferred embodiment of the invention includes a method for inhibiting natural killer cell proliferation. A highly preferred embodiment of the invention includes a method for stimulating natural killer cell differentiation. An alternative highly preferred embodiment of the invention includes a method for inhibiting natural killer cell differentiation. Highly preferred indications include neoplastic diseases (e.g., as described below under
	Kinase assay. Kinase assays, for example an Elk-1 kinase assay, for ERK signal transduction that regulate cell proliferation or differentiation are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote or inhibit cell proliferation, activation, and differentiation. Exemplary assays for ERK kinase activity that may be used or routinely modified to test ERK kinase-induced activity of polypeptides of the invention (including antibodies and agonists or antagonists of
·	Activation of Natural Killer Cell ERK Signaling Pathway.
	1141
	HFKET18
	193

Disorders"), blood disorders (e.g., as described below under	"Immune Activity", "Cardiovascular Disorders",	and/or "Blood-Related	Disorders"), immune disorders	(e.g., as described below under "Immune Activity") and		below under "Infectious	Disease"). Preferred	indications include blood	disorders (e.g., as described	below under "Immune	Activity", "Blood-Related	Disorders", and/or	"Cardiovascular Disorders").	Highly preferred indications	include autoimmune diseases	(e.g., rheumatoid arthritis,	systemic lupus erythematosis,	multiple sclerosis and/or as	described below) and	immunodeficiencies (e.g., as	described below). Additional	highly preferred indications	include inflammation and	inflammatory disorders.	Highly preferred indications	also include cancers such as,	kidney, melanoma, prostate,
assays disclosed in Forrer et al., Biol Chem 379(8-9):1101-	1110 (1998); Kyriakis JM,   Biochem Soc Symp 64:29-48	(1999); Chang and Karin,	Nature 410(6824):37-40	(2001); and Cobb MH, Frog Biophys Mol Biol 71(3-4):479-	500 (1999); the contents of	each of which are herein	incorporated by reference in its	entirety. Natural killer cells	that may be used according to	these assays are publicly	available (e.g., through the	ATCC). Exemplary natural	killer cells that may be used	according to these assays	include the human natural	killer cell lines (for example,	NK-YT cells which have	cytolytic and cytotoxic	activity) or primary NK cells.							\$	
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				oreast, lung, colon, pancreauc,
				esophageal, stomach, brain,
				liver, urinary cancer,
				lymphoma and leukemias.
	··-			Other preferred indications
				include benign dysproliferative
				disorders and pre-neoplastic
				conditions, such as, for
				example, hyperplasia,
				metaplasia, and/or dysplasia.
				Other highly preferred
				indications include,
				pancytopenia, leukopenia,
				leukemias, Hodgkin's disease,
				acute lymphocytic anemia
				(ALL), arthritis, asthma,
		-14		AIDS, granulomatous disease,
		~		inflammatory bowel disease,
				sepsis, psoriasis, immune
				reactions to transplanted
	_			organs and tissues,
				endocarditis, meningitis, Lyme
				Disease, and allergies.
HFKFG02	1142	Activation of	Kinase assay. Kinase assays,	A highly preferred
		Adipocyte ERK	for example an Elk-1 kinase	embodiment of the invention
		Signaling Pathway	assay, for ERK signal	includes a method for
	_		transduction that regulate cell	stimulating adipocyte
			proliferation or differentiation	proliferation. An alternative
			are well known in the art and	highly preferred embodiment
			may be used or routinely	of the invention includes a
	_		modified to assess the ability	method for inhibiting

indications include blood disorders (e.g., hypertension, congestive heart failure, blood	vessel blockage, heart disease, stroke, impotence and/or as	described below under "Immine Activity"	"Cardiovascular Disorders",	and/or "Blood-Related Disorders"), immune disorders	(e.g., as described below under	"Immune Activity"), neural	disorders (e.g., as described	below under "Neural Activity	and Neurological Diseases"),	and infection (e.g., as	described below under	"Infectious Disease").	A highly preferred indication	is diabetes mellitus. An	additional highly preferred	indication is a complication	associated with diabetes (e.g.,	diabetic retinopathy, diabetic	nephropathy, kidney disease	(e.g., renal failure,	nephropathy and/or other	diseases and disorders as	described in the "Renal	Disorders" section below),	diabetic neuropathy, nerve
assays are publicly available (e.g., through the ATCC).  Exemplary mouse adipocyte	cells that may be used according to these assays	include 3T3-L1 cells. 3T3-L1	preadipocyte cell line that is a	continuous substrain of 3T3 fibroblast cells developed	through clonal isolation and	undergo a pre-adipocyte to	adipose-like conversion under	appropriate differentiation	conditions known in the art.																

disease and nerve damage	(e.g., due to diabetic neuropathy) blood vessel	blockage, heart disease, stroke,	impotence (e.g., due to diabetic	neuropathy or blood vessel	blockage), seizures, mental	confusion, drowsiness,	nonketotic hyperglycemic-	hyperosmolar coma,	cardiovascular disease (e.g.,	heart disease, atherosclerosis,	microvascular disease,	hypertension, stroke, and other	diseases and disorders as	described in the	"Cardiovascular Disorders"	section below), dyslipidemia,	endocrine disorders (as	described in the "Endocrine	Disorders" section below),	neuropathy, vision impairment	(e.g., diabetic retinopathy and	blindness), ulcers and impaired	wound healing, infection (e.g.,	infectious diseases and	disorders as described in the	"Infectious Diseases" section	below (particularly of the	urinary tract and skin). An	additional highly preferred
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indication is obesity and/or	obesity. Additional highly	preferred indications include	weight loss or alternatively,	weight gain. Additional	highly preferred indications are	complications associated with	insulin resistance.	Additional highly preferred	indications are disorders of the	musculoskeletal systems	including myopathies,	muscular dystrophy, and/or as	described herein.	Additional highly preferred	indications include,	hypertension, coronary artery	disease, dyslipidemia,	gallstones, osteoarthritis,	degenerative arthritis, eating	disorders, fibrosis, cachexia,	and kidney diseases or	disorders. Preferred	indications include neoplasms	and cancer, such as,	lymphoma, leukemia and	breast, colon, and kidney	cancer. Additional preferred	indications include melanoma,	prostate, lung, pancreatic,
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								•																	_				
																							-7212						

esophageal, stomach, brain, liver, and urinary cancer. Highly preferred indications include lipomas and liposarcomas. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia.		Preferred indications include neoplastic diseases (e.g., as described below under "Hyperproliferative Disorders"), blood disorders (e.g., as described below under "Immune Activity", "Cardiovascular Disorders", and/or "Blood-Related Disorders"), and infection (e.g., an infectious disease as described below under "Infectious Disease"). Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below) and
		Assays for the activation of transcription through the AP1 response element are known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to modulate growth and other cell functions. Exemplary assays for transcription through the AP1 response element that may be used or routinely modified to test AP1-response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the
	IL-10 in Human T-cell 293T	Activation of transcription through AP1 response element in immune cells (such as T-cells).
	1142	1143
	HFKFG02	HFOXB13
	194	195

		,	invention) include assays	immunodeficiencies (e.g., as
			disclosed in Berger et al., Gene 66:1-10 (1988); Cullen and	described below). Additional highly preferred indications
			Malm, Methods in Enzymol	include inflammation and
			216:362-368 (1992); Henthorn	inflammatory disorders.
			et al., Proc Natl Acad Sci USA	Highly preferred indications
			85:6342-6346 (1988);	also include neoplastic
			Rellahan et al., J Biol Chem	diseases (e.g., leukemia,
			272(49):30806-30811 (1997);	lymphoma, and/or as described
			Chang et al., Mol Cell Biol	below under
			18(9):4986-4993 (1998); and	"Hyperproliferative
			Fraser et al., Eur J Immunol	Disorders"). Highly preferred
			29(3):838-844 (1999), the	indications include neoplasms
			contents of each of which are	and cancers, such as, leukemia,
			herein incorporated by	lymphoma, prostate, breast,
			reference in its entirety.	lung, colon, pancreatic,
		-	Mouse T cells that may be	esophageal, stomach, brain,
			used according to these assays	liver, and urinary cancer. Other
			are publicly available (e.g.,	preferred indications include
			through the ATCC).	benign dysproliferative
			Exemplary mouse T cells that	disorders and pre-neoplastic
			may be used according to these	conditions, such as, for
			assays include the HT2 cell	example, hyperplasia,
	200		line, which is an IL-2	metaplasia, and/or dysplasia.
			dependent suspension culture	Preferred indications include
 			cell line that also responds to	arthritis, asthma, AIDS,
			IL-4.	allergy, anemia, pancytopenia,
				leukopenia, thrombocytopenia,
				Hodgkin's disease, acute
	·			lymphocytic anemia (ALL),
				plasmacytomas, multiple

myeloma, Burkitt's lymphoma, granulomatous disease, inflammatory bowel disease, sepsis, psoriasis, suppression of immune reactions to transplanted organs and tissues, endocarditis, meningitis, and Lyme Disease.	Preferred embodiments of the invention include using polypeptides of the invention (or antibodies, agonists, or antagonists thereof) in detection, diagnosis, prevention, and/or treatment of asthma, allergy, hypersensitivity and inflammation.
	Caspase Apoptosis. Assays for caspase apoptosis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate caspase protease-mediated apoptosis in immune cells (such as, for example, in mast cells). Mast cells are found in connective and mucosal tissues throughout the body, and their activation via immunoglobulin E - antigen, promoted by T helper cell type 2 cytokines, is an important component of allergic disease. Dysregulation of mast cell apoptosis may play a role in allergic disease and mast cell tumor survival.
	Regulation of apoptosis of immune cells (such as mast cells).
	1144
	HFPAC12
	196

Exemplary assays for caspase apoptosis that may be used or routinely modified to test capase apoptosis activity induced by polypeptides of the invention (including antibodies	and agonists or antagonists of the invention) include the assays disclosed in: Masuda A, et al., J Biol Chem, 276(28):26107-26113 (2001); Yeatman CF 2nd, et al., J Exp Med, 192(8):1093-1103	(2000);Lee et al., FEBS Lett 485(2-3): 122-126 (2000); Nor et al., J Vasc Res 37(3): 209-218 (2000); and Karsan and Harlan, J Atheroscler Thromb 3(2): 75-80 (1996); the contents of each of which are herein incorporated by reference in its entirety.	according to these assays are publicly available (e.g., through commercial sources). Exemplary immune cells that may be used according to these assays include mast cells such as the HMC human mast cell line.

196	HFPAC12	1144	IFNg in Human T-cell 2B9		
196	HFPAC12	1144	IL-2 in Human T-cell 2B9		
	HFPA071	1145	Activation of JNK	Kinase assay. JNK kinase	Highly preferred indications
197			Signaling Pathway	assays for signal transduction	include asthma, allergy,
			in immune cells	that regulate cell proliferation,	hypersensitivity reactions,
			(such as	activation, or apoptosis are	inflammation, and
			eosinophils).	well known in the art and may	inflammatory disorders.
				be used or routinely modified	Additional highly preferred
				to assess the ability of	indications include immune
				polypeptides of the invention	and hematopoietic disorders
				(including antibodies and	(e.g., as described below under
				agonists or antagonists of the	"Immune Activity", and
				invention) to promote or	"Blood-Related Disorders"),
				inhibit cell proliferation,	autoimmune diseases (e.g.,
				activation, and apoptosis.	rheumatoid arthritis, systemic
				Exemplary assays for JNK	lupus erythematosis, Crohn"s
				kinase activity that may be	disease, multiple sclerosis
				used or routinely modified to	and/or as described below),
—, <u></u>				test JNK kinase-induced	immunodeficiencies (e.g., as
				activity of polypeptides of the	described below). Highly
				invention (including antibodies	preferred indications also
				and agonists or antagonists of	include boosting or inhibiting
				the invention) include the	immune cell proliferation.
				assays disclosed in Forrer et	Preferred indications include
				al., Biol Chem 379(8-9):1101-	neoplastic diseases (e.g.,
				1110 (1998); Gupta et al., Exp	leukemia, lymphoma, and/or as
				Cell Res 247(2): 495-504	described below under
		<b>19.</b> - 19 1		(1999); Kyriakis JM, Biochem	"Hyperproliferative
			3 3 3 3 3 3 3 3 3 3 3 3 3 3 3 3 3 3 3 3	Soc Symp 64:29-48 (1999);	Disorders"). Highly preferred

	nd eosinophil-mediated immune	4ol response, and suppressing an	9); eosinophil-mediated immune	ich response.			ec	says		.i.		d to		late		ys	ely	ity		odies	Jo 9					nd/or	Role	one-		
Chang and Karin, Nature	410(6824):37-40 (2001); and	Cobb MH, Prog Biophys Mol	Biol 71(3-4):479-500 (1999);	the contents of each of which	are herein incorporated by	reference in its entirety.	Exemplary cells that may be	used according to these assays	include eosinophils.	Eosinophils are important in	the late stage of allergic	reactions; they are recruited to	tissues and mediate the	inflammatory response of late	stage allergic reaction.	Moreover, exemplary assays	that may be used or routinely	modified to assess the ability	of polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) to modulate	signal transduction, cell	proliferation, activation, or	apoptosis in eosinophils	include assays disclosed and/or	cited in: Zhang JP, et al., "Role	of caspases in dexamethasone-	induced apoptosis and	activation of c-Jun NH2-

		Highly preferred indications include eosinophilia, asthma,	allergy, hypersensitivity reactions, inflammation, and
terminal kinase and p38 mitogen-activated protein kinase in human eosinophils" Clin Exp Immunol; Oct;122(1):20-7 (2000); Hebestreit H, et al., "Disruption of fas receptor signaling by nitric oxide in eosinophils" J Exp Med; Feb 2;187(3):415-25 (1998); J Allergy Clin Immunol 1999 Sep;104(3 Pt 1):565-74; and, Sousa AR, et al., "In vivo resistance to corticosteroids in bronchial asthma is associated with enhanced phosyphorylation of JUN N- terminal kinase and failure of prednisolone to inhibit JUN N- terminal kinase phosphorylation" J Allergy Clin Immunol; Sep;104(3 Pt 1):565-74 (1999); the contents of each of which are herein incomparated by reference in its	entirety.	Assay that measures the production of the chemokine	interleukin-8 (IL-8) from immune cells (such as the
	-	Production of IL-8 by immune cells	(such as the human EOL-1 eosinophil
	1 7 7	1145	
	TEDAGTI	HFFAU/I	
		197	

				line) are well known in the art (for example, measurement of IL-8 production by FMAT) and may be used or routinely	Additional highly preferred indications include immune and hematopoietic disorders (e.g., as described below under
			-	modified to assess the ability of polypeptides of the invention (including antibodies	"Immune Activity", and "Blood-Related Disorders"), autoimmune diseases (e.g.
				and agonists or antagonists of the invention) to promote or	rheumatoid arthritis, systemic lupus erythematosis, Crohn"s
· //*				inhibit. Eosinophils are a type of immune cell important in	disease, multiple sclerosis and/or as described below),
				allergic responses; they are recruited to tissues and	immunodeficiencies (e.g., as described below). Highly
				response of late stage allergic	preferred indications also include boosting or inhibiting
	eq			immunomodulator and may	Innimune cent profiteration.  Preferred indications include
				have a potential proinflammatory role in	neoplastic diseases (e.g., leukemia, lymphoma, and/or as
				immunological diseases and disorders (such as allergy and	described below under "Hyperproliferative
				asthma).	Disorders"). Highly preferred indications include boosting an
					eosinophil-mediated immune
					response, and suppressing an eosinophil-mediated immune
	HFPA071	1145	Production of IL-8	Assays measuring production	Highly preferred indications
197			by by endothelial	of IL-8 are well known in the	include immunological and
			cells (such as Human Umbilical	art and may be used or routinely modified to assess	inflammatory disorders (e.g., such as allergy, asthma.
					sacra as arres 2); assiring

Cord Endothelial the ability of polypeptides of cells).  Cells. the invention (including autibodies and agonists or regulate production and/or secretion of IL-8. For autibodies and agonists of the invention (including autibodies and agonists of autibodies and agonists of the invention (including autibodies and agonists of the invention (including autibodies and agonists of the invention) to secretion of IL-8 from endothelial cells (such as human umbilical vein cardiovascular disorders (e.g., HVVEC).  HUVECs are endothelial cells (HUVEC)).  HUVECs are endothelial cells (HUVEC)).  Avessels, and are involved in functions that include, but are not limited to, angiogenesis, vascular permeability, vascular consequent complications initiation and perpetuation of resulting from septic shock), inflammation and secretion of IL-8 may play an important and
the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate production and/or secretion of IL-8. For example, FMAT may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate production and/or secretion of IL-8 from endothelial cells (such as human umbilical vein endothelial cells (HUVEC)). HUVECs are endothelial cells which line venous blood vessels, and are involved in functions that include, but are not limited to, angiogenesis, vascular permeability, vascular tone, and immune cell extravasation. Endothelial cells play a pivotal role in the initiation and perpetuation of inflammation and secretion of IL-8 may play an important role in recruitment and
the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate production and/or secretion of IL-8. For example, FMAT may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate production and/or secretion of IL-8 from endothelial cells (such as human umbilical vein endothelial cells (HUVEC)). HUVECs are endothelial cells which line venous blood vessels, and are involved in functions that include, but are not limited to, angiogenesis, vascular permeability, vascular tone, and immune cell extravasation. Endothelial cells play a pivotal role in the initiation and perpetuation of inflammation and secretion of IL-8 may play an important role in recruitment and
the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate production and/or secretion of IL-8. For example, FMAT may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate production and/or secretion of IL-8 from endothelial cells (such as human umbilical vein endothelial cells (HUVEC)). HUVECs are endothelial cells which line venous blood vessels, and are involved in functions that include, but are not limited to, angiogenesis, vascular permeability, vascular tone, and immune cell extravasation. Endothelial cells play a pivotal role in the initiation and perpetuation of inflammation and secretion of IL-8 may play an important role in recruitment and
Cells).
Cells).
Cells

				such as neutrophils,	
				macrophages, and	
				lymphocytes.	
	HFPCX09	1146	Production of TNF	TNFa FMAT. Assays for	A highly preferred
198			alpha by dendritic	immunomodulatory proteins	embodiment of the invention
			cells	produced by activated	includes a method for
				macrophages, T cells,	inhibiting (e.g., decreasing)
				fibroblasts, smooth muscle,	TNF alpha production. An
				and other cell types that exert a	alternative highly preferred
				wide variety of inflammatory	embodiment of the invention
				and cytotoxic effects on a	includes a method for
				variety of cells are well known	stimulating (e.g., increasing)
				in the art and may be used or	TNF alpha production.
_				routinely modified to assess	Highly preferred indications
		,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,		the ability of polypeptides of	include blood disorders (e.g.,
				the invention (including	as described below under
				antibodies and agonists or	"Immune Activity", "Blood-
		142		antagonists of the invention) to	Related Disorders", and/or
				mediate immunomodulation,	"Cardiovascular Disorders"),
				modulate inflammation and	Highly preferred indications
				cytotoxicity. Exemplary	include autoimmune diseases
				assays that test for	(e.g., rheumatoid arthritis,
				immunomodulatory proteins	systemic lupus erythematosis,
				evaluate the production of	Crohn"s disease, multiple
				cytokines such as tumor	sclerosis and/or as described
				necrosis factor alpha (TNFa),	below), immunodeficiencies
		******		and the induction or inhibition	(e.g., as described below),
	-,			of an inflammatory or	boosting a T cell-mediated
				cytotoxic response. Such	immune response, and
				assays that may be used or	suppressing a T cell-mediated
				routinely modified to test	immune response. Additional

highly preferred indications include inflammation and inflammatory disorders, and treating joint damage in	patients with rheumatoid arthritis. An additional highly preferred indication is sepsis.	Highly preferred indications include neoplastic diseases (e.g., leukemia, lymphoma,	and/or as described below under "Hyperproliferative Disorders") Additionally	highly preferred indications include neoplasms and	cancers, such as, leukemia, lymphoma, melanoma, elioma	(e.g., malignant glioma), solid tumors, and prostate, breast,	lung, colon, pancreatic, esophageal, stomach, brain,	liver and urinary cancer. Other preferred indications include	benign dysproliferative disorders and pre-neoplastic	conditions, such as, for example, hyperplasia.	metaplasia, and/or dysplasia.	anemia, pancytopenia, leukopenia, thrombocytopenia.
immunomodulatory activity of polypeptides of the invention (including antibodies and agonists or antagonists of the	invention) include assays disclosed in Miraglia et al., J Biomolecular Screening 4:193-	204(1999); Rowland et al., "Lymphocytes: a practical approach" Chapter 6:138-160	(2000); Verhasselt et al., Eur J Immunol 28(11):3886-3890 (1198): Dahlen et al. 1	Immunol 160(7):3585-3593 (1998); Verhasselt et al., J	Immunol 158:2919-2925 (1997); and Nardelli et al J	Leukoc Biol 65:822-828 (1999), the contents of each of	which are herein incorporated by reference in its entirety.	Human dendritic cells that may be used according to these	assays may be isolated using techniques disclosed herein or	otherwise known in the art. Human dendritic cells are	antigen presenting cells in	when activated by antigen and/or cytokines, initiate and
	···							_				

			and functional activities.	lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, cardiac reperfusion injury, and asthma and allergy. An additional preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease").
HFPCX09	1146	Activation of transcription through GATA-3 response element in immune cells (such as mast cells).	This reporter assay measures activation of the GATA-3 signaling pathway in HMC-1 human mast cell line. Activation of GATA-3 in mast cells has been linked to cytokine and chemokine production. Assays for the activation of transcription through the GATA3 response element are well-known in the	Highly preferred indications include allergy, asthma, and rhinitis. Additional preferred indications include infection (e.g., an infectious disease as described below under "Infectious Disease"), and inflammation and inflammatory disorders. Preferred indications also include blood disorders (e.g.,

		art and may be used or	se described below under
		air aina may oc asca or	as acsertoca octow anaci
		routinely modified to assess	"Immune Activity", "Blood-
		the ability of polypeptides of	Related Disorders", and/or
		the invention (including	"Cardiovascular Disorders").
		antibodies and agonists or	Preferred indications include
-		antagonists of the invention) to	autoimmune diseases (e.g.,
		regulate GATA3 transcription	rheumatoid arthritis, systemic
		factors and modulate	lupus erythematosis, multiple
		expression of mast cell genes	sclerosis and/or as described
		important for immune response	below) and
		development. Exemplary	immunodeficiencies (e.g., as
		assays for transcription	described below). Preferred
		through the GATA3 response	indications include neoplastic
		element that may be used or	diseases (e.g., leukemia,
		routinely modified to test	lymphoma, melanoma,
		GATA3-response element	prostate, breast, lung, colon,
		activity of polypeptides of the	pancreatic, esophageal,
		invention (including antibodies	stomach, brain, liver, and
		and agonists or antagonists of	urinary tract cancers and/or as
		the invention) include assays	described below under
		disclosed in Berger et al., Gene	"Hyperproliferative
		66:1-10 (1998); Cullen and	Disorders"). Other preferred
		Malm, Methods in Enzymol	indications include benign
		216:362-368 (1992); Henthorn	dysproliferative disorders and
		et al., Proc Natl Acad Sci USA	pre-neoplastic conditions, such
		85:6342-6346 (1988); Flavell	as, for example, hyperplasia,
		et al., Cold Spring Harb Symp	metaplasia, and/or dysplasia.
		Quant Biol 64:563-571 (1999);	Preferred indications include
		Rodriguez-Palmero et al., Eur	anemia, pancytopenia,
		J Immunol 29(12):3914-3924	leukopenia, thrombocytopenia,
		(1999); Zheng and Flavell,	leukemias, Hodgkin's disease,

				Cell 89(4):587-596 (1997); and	acute lymphocytic anemia
				Henderson et al., Mol Cell Biol	(ALL), plasmacytomas,
				14(6):4286-4294 (1994), the	multiple myeloma, Burkitt's
				contents of each of which are	lymphoma, arthritis, AIDS,
				herein incorporated by	granulomatous disease,
				reference in its entirety. Mast	inflammatory bowel disease,
				cells that may be used	sepsis, neutropenia,
				according to these assays are	neutrophilia, psoriasis,
				publicly available (e.g.,	suppression of immune
				through the ATCC).	reactions to transplanted
				Exemplary human mast cells	organs and tissues, hemophilia,
				that may be used according to	hypercoagulation, diabetes
				these assays include the HMC-	mellitus, endocarditis,
				1 cell line, which is an	meningitis, and Lyme Disease.
				immature human mast cell line	
				established from the peripheral	
				blood of a patient with mast	
				cell leukemia, and exhibits	
				many characteristics of	
				immature mast cells.	
	HFPCX09	1146	Activation of	This reporter assay measures	Highly preferred indications
198			transcription	activation of the NFAT	include allergy, asthma, and
			through NFAT	signaling pathway in HMC-1	rhinitis. Additional preferred
			response element in	human mast cell line.	indications include infection
			immune cells (such	Activation of NFAT in mast	(e.g., an infectious disease as
			as mast cells).	cells has been linked to	described below under
				cytokine and chemokine	"Infectious Disease"), and
				production. Assays for the	inflammation and
				activation of transcription	inflammatory disorders.
-				through the Nuclear Factor of	Preferred indications also
				Activated T cells (NFAT)	include blood disorders (e.g.,

as described below under "Immune Activity", "Blood- Related Disorders", and/or	"Cardiovascular Disorders"). Preferred indications include autoimmune diseases (e.g	rheumatoid arthritis, systemic lupus erythematosis, multiple	sclerosis and/or as described below) and	immunodeficiencies (e.g., as described below). Preferred	indications include neoplastic	diseases (e.g., leukemia, lymphoma, melanoma,	prostate, breast, lung, colon,	pancreatic, esophageal,	stomach, brain, liver, and	urinary tract cancers and/or as	described below under "Hyperproliferative"	Disorders"). Other preferred		dysproliferative disorders and	pre-neoplastic conditions, such	as, for example, hyperplasia,	metaplasia, and/or dysplasia.	Preferred indications include	anemia, pancytopenia,	leukopenia, thrombocytopenia,	leukemias, Hodgkin's disease,
response element are well- known in the art and may be used or routinely modified to	assess the ability of polypeptides of the invention (including antibodies and	agonists or antagonists of the invention) to regulate NFAT	transcription factors and modulate expression of genes	involved in immunomodulatory functions.	Exemplary assays for	transcription through the NFAT response element that	may be used or routinely	modified to test NFAT-	response element activity of	polypeptides of the invention	(including antibodies and agonists of the	invention) include assays	disclosed in Berger et al., Gene	66:1-10 (1998); Cullen and	Malm, Methods in Enzymol	216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA	85:6342-6346 (1988); De Boer	et al., Int J Biochem Cell Biol	31(10):1221-1236 (1999); Ali	et al., J Immunol
				<b>N</b> -2-1															-		

				165(12):7215-7223 (2000):	acute lymphocytic anemia
	-			Hutchinson and McCloskey, J	(ALL), plasmacytomas
				Biol Chem 270(27):16333-	multiple myeloma, Burkitt's
				16338 (1995), and Turner et	lymphoma, arthritis, AIDS,
				al., J Exp Med 188:527-537	granulomatous disease,
				(1998), the contents of each of	inflammatory bowel disease,
				which are herein incorporated	sepsis, neutropenia,
	_			by reference in its entirety.	neutrophilia, psoriasis,
		- Au		Mast cells that may be used	suppression of immune
				according to these assays are	reactions to transplanted
				publicly available (e.g.,	organs and tissues, hemophilia,
				through the ATCC).	hypercoagulation, diabetes
				Exemplary human mast cells	mellitus, endocarditis,
	-			that may be used according to	meningitis, and Lyme Disease.
				these assays include the HMC-	
-				1 cell line, which is an	
				immature human mast cell line	
				established from the peripheral	
				blood of a patient with mast	
				cell leukemia, and exhibits	
				many characteristics of	
				immature mast cells.	
198	HFPCX09	1146	VEGF in HT1080		
	HFPCX09	1146	IL-12 in Human B	- Andrews	100
198			cells		
	HFPCX09	1146	IFNg in Human T-		
198			cell 293T		
	HFPCX09	1146	IL-2 in Human T-		
198		200	cell 293T		
	HFPCX36	1147	SEAP in		

199			Senescence Assay		
	HFPCX36	1147	Activation of	Assays for the activation of	Highly preferred indications
199			transcription	transcription through the	include inflammation and
			through NFKB	NFKB response element are	inflammatory disorders.
			response element in	well-known in the art and may	Highly preferred indications
			immune cells (such	be used or routinely modified	include blood disorders (e.g.,
			as T-cells).	to assess the ability of	as described below under
				polypeptides of the invention	"Immune Activity", "Blood-
				(including antibodies and	Related Disorders", and/or
				agonists or antagonists of the	"Cardiovascular Disorders").
				invention) to regulate NFKB	Highly preferred indications
				transcription factors and	include autoimmune diseases
				modulate expression of	(e.g., rheumatoid arthritis,
				immunomodulatory genes.	systemic lupus erythematosis,
				Exemplary assays for	multiple sclerosis and/or as
				transcription through the	described below), and
				NFKB response element that	immunodeficiencies (e.g., as
				may be used or rountinely	described below). An
				modified to test NFKB-	additional highly preferred
			~ <del>-</del>	response element activity of	indication is infection (e.g.,
				polypeptides of the invention	AIDS, and/or an infectious
				(including antibodies and	disease as described below
	-			agonists or antagonists of the	under "Infectious Disease").
				invention) include assays	Highly preferred indications
				disclosed in Berger et al., Gene	include neoplastic diseases
				66:1-10 (1998); Cullen and	(e.g., melanoma, leukemia,
,				Malm, Methods in Enzymol	lymphoma, and/or as described
				216:362-368 (1992); Henthorn	below under
				et al., Proc Natl Acad Sci USA	"Hyperproliferative
				85:6342-6346 (1988); Black et	Disorders"). Highly preferred
				al., Virus Gnes 15(2):105-117	indications include neoplasms

and cancers, such	as,melanoma, renal cell	carcinoma, leukemia,	lymphoma, and prostate,	breast, lung, colon, pancreatic,	esophageal, stomach, brain,	liver and urinary cancer. Other	preferred indications include	benign dysproliferative	disorders and pre-neoplastic	conditions, such as, for	example, hyperplasia,	metaplasia, and/or dysplasia.	Preferred indications also	include anemia, pancytopenia,	leukopenia, thrombocytopenia,	Hodgkin's disease, acute	lymphocytic anemia (ALL),	plasmacytomas, multiple	myeloma, Burkitt's lymphoma,	arthritis, AIDS,	granulomatous disease,	inflammatory bowel disease,	sepsis, neutropenia,	neutrophilia, psoriasis,	hemophilia, hypercoagulation,	diabetes mellitus, endocarditis,	meningitis, Lyme Disease,	suppression of immune	reactions to transplanted	organs, asthma and allergy.
(1997); and Fraser et al.,	29(3):838-844 (1999), the	contents of each of which are	herein incorporated by	reference in its entirety. T	cells that may be used	according to these assays are	publicly available (e.g.,	through the ATCC).	Exemplary human T cells that	may be used according to these	assays include the SUPT cell	line, which is a suspension	culture of IL-2 and IL-4	responsive T cells.																
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ш		HFRAN90	1148	Activation of	Assavs for the activation of	Highly preferred indications
	200			transcription	transcription through the	include neonlastic diseases
	_			through GAS	Gamma Interferon Activation	(e.g., leukemia, lymphoma,
	_			response element in	Site (GAS) response element	and/or as described below
				immune cells (such	are well-known in the art and	under "Hyperproliferative
				as T-cells).	may be used or routinely	Disorders"). Highly preferred
					modified to assess the ability	indications include neoplasms
	-				of polypeptides of the	and cancers, such as, for
					invention (including antibodies	example, leukemia, lymphoma
					and agonists or antagonists of	(e.g., T cell lymphoma,
					the invention) to regulate	Burkitt's lymphoma, non-
					STAT transcription factors and	Hodgkins lymphoma,
					modulate gene expression	Hodgkin"s disease),
					involved in a wide variety of	melanoma, and prostate,
					cell functions. Exemplary	breast, lung, colon, pancreatic,
120					assays for transcription	esophageal, stomach, brain,
	_				through the GAS response	liver and urinary cancer. Other
					element that may be used or	preferred indications include
					routinely modified to test	benign dysproliferative
					GAS-response element activity	disorders and pre-neoplastic
					of polypeptides of the	conditions, such as, for
					invention (including antibodies	example, hyperplasia,
					and agonists or antagonists of	metaplasia, and/or dysplasia.
				-	the invention) include assays	Preferred indications include
					disclosed in Berger et al., Gene	autoimmune diseases (e.g.,
					66:1-10 (1998); Cullen and	rheumatoid arthritis, systemic
					Malm, Methods in Enzymol	lupus erythematosis, multiple
					216:362-368 (1992); Henthorn	sclerosis and/or as described
					et al., Proc Natl Acad Sci USA	below), immunodeficiencies
					85:6342-6346 (1988);	(e.g., as described below),
					Matikainen et al., Blood	boosting a T cell-mediated

Henttinen et al., 1 Immunol 155(10):4582-4587 (1995), the contents of each of which are reference in its entirety.  Exemplary human T cells, such as the MOLT4 cell line, these assays are publicly available (e.g., through the ATCC).  ATCC).  ATCC).  Related Disorders", and infection (e.g., viral infections, tuberculosis, infections, tuberculosis, infections, tuberculosis, infections, tuberculosis, infections associated with chromic granulomatosus disease and malignant osteoporosis, and/or an infectious disease as described below under "Infectious Diseases"). An additional preferred indication is idiopathic pulmonary fibrosis. Preferred indications is idiopathic pulmonary fibrosis. AILD, plasmacytomas, multiple myelomagnus, incured acute lymphocytic anemia (ALL), plasmacytomas, multiple myelomagnus include acute lymphocytic anemia (ALL), plasmacytomas, multiple myelomagnus include acute lymphocytic anemia (ALL), plasmacytomas, multiple myelomagnus include acute lymphocytic anemia (ALL), plasmacytomas,
93(6):1980-1991 (1999); and Henttinen et al., J Immunol 155(10):4582-4587 (1995), the contents of each of which are herein incorporated by reference in its entirety. Exemplary human T cells, such as the MOLT4 cell line, that may be used according to these assays are publicly available (e.g., through the ATCC).
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sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, and asthma and allergy.	Preferred embodiments of the invention include using polypeptides of the invention (or antibodies, agonists, or antagonists thereof) in detection, diagnosis, prevention, and/or treatment of Inflammation, Vascular Disease, Athereosclerosis, Restenosis, and Stroke
	Assays for measuring expression of ICAM-1 are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate ICAM-1 expression. Exemplary assays that may be used or routinely modified to measure ICAM-1 expression include assays disclosed in: Takacs P, et al, FASEB J, 15(2):279-281 (2001); and, Miyamoto K, et al., Am J Pathol, 156(5):1733-1739 (2000), the contents of each of which is herein incorporated by reference in its entirety. Cells that may be used according to these assays
	Production of ICAM-1
	1148
	HFRAN90
	200

	Preferred embodiments of the invention include using polypeptides of the invention (or antibodies, agonists, or antagonists thereof) in detection, diagnosis, prevention, and/or treatment of Neurological Diseases and Disorders (e.g. Alzheimer"s Disease, Parkinson's Disease, Brain Cancer, Seizures).	
are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary cells that may be used according to these assays include microvascular endothelial cells (MVEC).	Assays for the activation of transcription through the NFKB response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate NFKB transcription factors and modulate expression of neuronal genes. Exemplary assays for transcription through the NFKB response element that may be used or routinely modified to test	activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in: Gill JS, et al., Neurobiol Dis 7(4):448-461
	Activation of transcription through NFKB response element in neuronal cells (such as SKNMC cells).	
	1149	
	HFTCU19	
	201	

				(2000); Tamatani M, et al., J	
				Biol Chem, 274(13):8531-	
				8538 (1999); Berger et al.,	
				Gene 66:1-10 (1998); Cullen	
				and Malm, Methods in	
				Enzymol 216:362-368 (1992);	
				Henthorn et al., Proc Natl	
	12 N			Acad Sci USA 85:6342-6346	
				(1988); Valle Blazquez et al,	
				Immunology 90(3):455-460	
				(1997); Aramburau et al., J	
				Exp Med 82(3):801-810	
				(1995); and Fraser et al.,	
-		** ·		29(3):838-844 (1999), the	
				contents of each of which are	
				herein incorporated by	
		•		reference in its entirety.	
				Neuronal cells that may be	
				used according to these assays	
				are publicly available (e.g.,	
				through the ATCC).	
				Exemplary neuronal cells that	
				may be used according to these	
				assays include the SKNMC	
				neuronal cell line.	
	HFTDL56	1150	Activation of	Assays for the activation of	A preferred embodiment of
202			transcription	transcription through the	the invention includes a
			through serum	Serum Response Element	method for inhibiting (e.g.,
			response element in	(SRE) are well-known in the	reducing) TNF alpha
			immune cells (such	art and may be used or	production. An alternative
			as T-cells).	routinely modified to assess	preferred embodiment of the

invention includes a method for stimulating (e.g., increasing) TNF alpha production. Preferred	indications include blood disorders (e.g., as described below under "Immune	Activity", "Blood-Related Disorders", and/or	"Cardiovascular Disorders"), Highly preferred indications	include autoimmune diseases (e.g., rheumatoid arthritis,	systemic lupus erythematosis,	sclerosis and/or as described	below), immunodeficiencies	(e.g., as described below),	boosting a L cell-mediated	suppressing a T cell-mediated	immune response. Additional	highly preferred indications	include inflammation and	inflammatory disorders, and	treating joint damage in	patients with rheumatoid	arthritis. An additional highly	preferred indication is sepsis.	Highly preferred indications	include neoplastic diseases
the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to	regulate the serum response factors and modulate the expression of genes involved	in growth. Exemplary assays for transcription through the	SRE that may be used or routinely modified to test SRE	activity of the polypeptides of the invention (including	antibodies and agonists or	include assays disclosed in	Berger et al., Gene 66:1-10	(1998); Cullen and Malm,	Methods in Enzymol 216:362-   368 (1992): Henthorn et al	Proc Natl Acad Sci USA	85:6342-6346 (1988); and	Black et al., Virus Genes	12(2):105-117 (1997), the	content of each of which are	herein incorporated by	reference in its entirety. T	cells that may be used	according to these assays are	publicly available (e.g.,	through the ATCC).
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(e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Additionally	highly preferred indications include neoplasms and	leukemia, lymphoma, melanoma, glioma (e.g.,	tumors, and prostate, breast, lung, colon, pancreatic,	esophageal, stomach, brain, liver and urinary cancer. Other	preferred indications include benign dysproliferative disorders and pre-neonlastic	conditions, such as, for example, hyperplasia,	metaplasia, and/or dysplasia. Preferred indications include	anemia, pancytopenia, leukopenia, thrombocytopenia,	Hodgkin's disease, acute lymphocytic anemia (ALL),	plasmacytomas, multiple myeloma, Burkitt's lymphoma,	arthritis, AIDS, granulomatous	disease, inflammatory bowel	neutrophilia, psoriasis.
Exemplary mouse T cells that may be used according to these assays include the CTLL cell line, which is an II2	dependent suspension culture of T cells with cytotoxic	activity.											

suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, cardiac reperfusion injury, and asthma and allergy. An additional preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease").		Preferred embodiments of the invention include using polypeptides of the invention (or antibodies, agonists, or antagonists thereof) in detection, diagnosis, prevention, and/or treatment of Inflammation, Vascular Disease, Athereosclerosis, Restenosis, and Stroke
		Assays for measuring expression of ICAM-1 are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate ICAM-1 expression. Exemplary assays that may be used or routinely modified to measure ICAM-1 expression include assays disclosed in: Takacs P, et al, FASEB J, 15(2):279-281 (2001); and, Miyamoto K, et al., Am J Pathol, 156(5):1733-
	IL-6 in HUVEC	Production of ICAM-1
	1150	1150
	HFTDL56	HFTDL56
	202	202

		A highly motornood	antodim ted	embodiment of the invention	includes a method for	stimulating endothelial cell	growth. An alternative highly	preferred embodiment of the	invention includes a method	for inhibiting endothelial cell	growth. A highly preferred	embodiment of the invention	includes a method for	stimulating endothelial cell	proliferation. An alternative	highly preferred embodiment	of the invention includes a	method for inhibiting	endothelial cell proliferation.
each of which is herein incorporated by reference in its entirety. Cells that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary cells that may be used according to these assays include microvascular endothelial cells (MVEC).		Caspase Apontosis Bessue	Account the posting amountain	Assays for caspase apoptosis	rescue are well known in the	art and may be used or	routinely modified to assess	the ability of the polypeptides	of the invention (including	antibodies and agonists or	antagonists of the invention) to	inhibit caspase protease-	mediated apoptosis.	Exemplary assays for caspase	apoptosis that may be used or	routinely modified to test	caspase apoptosis rescue of	polypeptides of the invention	(including antibodies and
	SEAP in UMR-106	Protection from	Endothelial Cell	Amontosia Coll	Apoptosis.						-		-						
	1150	1151																	
	HFTDL56	HFTDZ36																	
	202		203															-	

of the invention includes a	method for inducing cardiac	hypertrophy. Highly	preferred indications include	neoplastic diseases (e.g., as	described below under	"Hyperproliferative	Disorders"), and disorders of	the cardiovascular system	(e.g., heart disease, congestive	heart failure, hypertension,	aortic stenosis,	cardiomyopathy, valvular	regurgitation, left ventricular	dysfunction, atherosclerosis	and atherosclerotic vascular	disease, diabetic nephropathy,	intracardiac shunt, cardiac	hypertrophy, myocardial	infarction, chronic	hemodynamic overload, and/or	as described below under	"Cardiovascular Disorders").	Highly preferred indications	include cardiovascular,	endothelial and/or angiogenic	disorders (e.g., systemic	disorders that affect vessels	such as diabetes mellitus, as	well as diseases of the vessels	41
			-																			-								

indications include benign	dysproliferative disorders and	pre-neoplastic conditions, such	as, for example, hyperplasia,	metaplasia, and/or dysplasia.	Highly preferred indications	also include arterial disease,	such as, atherosclerosis,	hypertension, coronary artery	disease, inflammatory	vasculitides, Reynaud's	disease and Reynaud"s	phenomenom, aneurysms,	restenosis; venous and	lymphatic disorders such as	thrombophlebitis,	lymphangitis, and	lymphedema; and other	vascular disorders such as	peripheral vascular disease,	and cancer. Highly	preferred indications also	include trauma such as	wounds, burns, and injured	tissue (e.g., vascular injury	such as, injury resulting from	balloon angioplasty, and	atheroschlerotic lesions),	implant fixation, scarring,	ischemia reperfusion injury,	rheumatoid arthritis.
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ase, renal	e renal	osis.	eferred	troke,	tic or	hrombotic	ders,		disorders,		atment	etriosis	·s	ferred	bromas,	arrest,	pu	Preferred	poo	cribed	•	lated	_	rders").	include	(e.g.,	systemic	multiple	scribed	
cerebrovascular disease, renal	diseases such as acute renal	failure, and osteoporosis.	Additional highly preferred	indications include stroke,	graft rejection, diabetic or	other retinopathies, thrombotic	and coagulative disorders,	vascularitis, lymph	angiogenesis, sexual disorders,	age-related macular	degeneration, and treatment	/prevention of endometriosis	and related conditions.	Additional highly preferred	indications include fibromas,	heart disease, cardiac arrest,	heart valve disease, and	vascular disease.	indications include blood	disorders (e.g., as described	below under "Immune	Activity", "Blood-Related	ers", and/or	"Cardiovascular Disorders").	Preferred indications include	autoimmune diseases (e.g.,	rheumatoid arthritis, systemic	lupus erythematosis, multiple	sclerosis and/or as described	and
cerebr	diseas	failure	Additi	indica	graft r	other	and co	vascul	angiog	age-re	degene	/preve	and rel	Addition	indicat	heart d	heart v	vascul	indicat	disorde	below	Activit	Disord	"Cardio	Preferr	autoim	rhenms	lupus e	scleros	below) and
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		Exemplary assays that may be	blockage), seizures, mental
		used or routinely modified to	confusion, drowsiness,
		test for stimulation of insulin	nonketotic hyperglycemic-
		secretion (from pancreatic	hyperosmolar coma,
		cells) by polypeptides of the	cardiovascular disease (e.g.,
		invention (including antibodies	heart disease, atherosclerosis,
		and agonists or antagonists of	microvascular disease,
		the invention) include assays	hypertension, stroke, and other
		disclosed in: Ahren, B., et al.,	diseases and disorders as
		Am J Physiol, 277(4 Pt	described in the
		2):R959-66 (1999); Li, M., et	"Cardiovascular Disorders"
		al., Endocrinology,	section below), dyslipidemia,
		138(9):3735-40 (1997); Kim,	endocrine disorders (as
		K.H., et al., FEBS Lett,	described in the "Endocrine
		377(2):237-9 (1995); and,	Disorders" section below),
		Miraglia S et. al., Journal of	neuropathy, vision impairment
		Biomolecular Screening,	(e.g., diabetic retinopathy and
		4:193-204 (1999), the contents	blindness), ulcers and impaired
*****		of each of which is herein	wound healing, and infection
		incorporated by reference in its	(e.g., infectious diseases and
		entirety. Pancreatic cells that	disorders as described in the
		may be used according to these	"Infectious Diseases" section
		assays are publicly available	below, especially of the
		(e.g., through the ATCC)	urinary tract and skin), carpal
		and/or may be routinely	tunnel syndrome and
		generated. Exemplary	Dupuytren's contracture).
		pancreatic cells that may be	An additional highly preferred
		used according to these assays	indication is obesity and/or
		include rat INS-1 cells. INS-1	complications associated with
		cells are a semi-adherent cell	obesity. Additional highly
		line established from cells	preferred indications include

ed weight loss or alternatively,  weight gain. Aditional highly preferred indications are complications associated with insulin resistance.					A highly preferred embodiment of the invention includes a method for stimulating endothelial cell growth. An alternative highly preferred embodiment of the invention includes a method for inhibiting endothelial cell growth. A highly preferred embodiment of the invention includes a method for stimulating endothelial cell proliferation. An alternative highly preferred embodiment
isolated from an X-ray induced rat transplantable insulinoma. These cells retain characteristics typical of native pancreatic beta cells including glucose inducible insulin secretion. References: Asfari et al. Endocrinology 1992 130:167.					Kinase assay. JNK and p38 kinase assays for signal transduction that regulate cell proliferation, activation, or apoptosis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote or inhibit cell proliferation, activation, and anontosis. Exemplary assays
	SEAP in Jurkat/IL4 promoter	Hexosaminidase in RBL-2H3	IL-8 in SW480	SEAP in SW480	Activation of Endothelial Cell p38 or JNK Signaling Pathway.
	1152	1152	1152	1152	1153
	HFVAB79	HFVAB79	HFVAB79	HFVAB79	HFVGE32
	204	204	204	204	205

		for INK and p38 kinase	of the invention includes a
		activity that may be used or	method for inhibiting
		routinely modified to test JNK	endothelial cell proliferation.
		and p38 kinase-induced	A highly preferred
		activity of polypeptides of the	embodiment of the invention
		invention (including antibodies	includes a method for
		and agonists or antagonists of	stimulating apoptosis of
		the invention) include the	endothelial cells. An
		assays disclosed in Forrer et	alternative highly preferred
		al., Biol Chem 379(8-9):1101-	embodiment of the invention
		1110 (1998); Gupta et al., Exp	includes a method for
		Cell Res 247(2): 495-504	inhibiting (e.g., decreasing)
		(1999); Kyriakis JM, Biochem	apoptosis of endothelial cells.
		Soc Symp 64:29-48 (1999);	A highly preferred
		Chang and Karin, Nature	embodiment of the invention
		410(6824):37-40 (2001); and	includes a method for
		Cobb MH, Prog Biophys Mol	stimulating (e.g., increasing)
		Biol 71(3-4):479-500 (1999);	endothelial cell activation. An
		the contents of each of which	alternative highly preferred
		are herein incorporated by	embodiment of the invention
		reference in its entirety.	includes a method for
-	-	Endothelial cells that may be	inhibiting (e.g., decreasing) the
		used according to these assays	activation of and/or
		are publicly available (e.g.,	inactivating endothelial cells.
		through the ATCC).	A highly preferred
		Exemplary endothelial cells	embodiment of the invention
		that may be used according to	includes a method for
		these assays include human	stimulating angiogenisis. An
		umbilical vein endothelial cells	alternative highly preferred
		(HUVEC), which are	embodiment of the invention
		endothelial cells which line	includes a method for

inhibiting angiogenesis. A highly preferred embodiment	of the invention includes a	method for reducing cardiac	hypertrophy. An alternative	highly preferred embodiment	of the invention includes a	method for inducing cardiac	hypertrophy. Highly	preferred indications include	neoplastic diseases (e.g., as	described below under	"Hyperproliferative	Disorders"), and disorders of	the cardiovascular system	(e.g., heart disease, congestive	heart failure, hypertension,	aortic stenosis,	cardiomyopathy, valvular	regurgitation, left ventricular	dysfunction, atherosclerosis	and atherosclerotic vascular	disease, diabetic nephropathy,	intracardiac shunt, cardiac	hypertrophy, myocardial	infarction, chronic	hemodynamic overload, and/or	as described below under	"Cardiovascular Disorders").	Highly preferred indications	include cardiovascular,
venous blood vessels, and are involved in functions that	include, but are not limited to,	angiogenesis, vascular	permeability, vascular tone,	and immune cell extravasation.																									

endothelial and/or angiogenic	disorders (e.g., systemic	disorders that affect vessels	such as diabetes mellitus, as	well as diseases of the vessels	themselves, such as of the	arteries, capillaries, veins	and/or lymphatics). Highly	preferred are indications that	stimulate angiogenesis and/or	cardiovascularization. Highly	preferred are indications that	inhibit angiogenesis and/or	cardiovascularization.	Highly preferred indications	include antiangiogenic activity	to treat solid tumors,	leukemias, and Kaposi"s	sarcoma, and retinal disorders.	Highly preferred indications	include neoplasms and cancer,	such as, Kaposi"s sarcoma,	hemangioma (capillary and	cavernous), glomus tumors,	telangiectasia, bacillary	angiomatosis,	hemangioendothelioma,	angiosarcoma,	haemangiopericytoma,	lymphangioma,	lymphangiosarcoma. Highly
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		-			MT Y																									

preferred indications also	include cancers such as, prostate, breast, lung, colon,	pancreatic, esophageal,	stomach, brain, liver, and	urinary cancer. Preferred	indications include benign	dysproliferative disorders and	pre-neoplastic conditions, such	as, for example, hyperplasia,	metaplasia, and/or dysplasia.	Highly preferred indications	also include arterial disease,	such as, atherosclerosis,	hypertension, coronary artery	disease, inflammatory	vasculitides, Reynaud's	disease and Reynaud"s	phenomenom, aneurysms,	restenosis; venous and	lymphatic disorders such as	thrombophlebitis,	lymphangitis, and	lymphedema; and other	vascular disorders such as	peripheral vascular disease,	and cancer. Highly	preferred indications also	include trauma such as	wounds, burns, and injured	tissue (e.g., vascular injury
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								-													- 114								

such as, injury resulting from	balloon angioplasty, and	atheroschlerotic lesions),	implant fixation, scarring,	ischemia reperfusion injury,	rheumatoid arthritis,	cerebrovascular disease, renal	diseases such as acute renal	failure, and osteoporosis.	Additional highly preferred	indications include stroke,	graft rejection, diabetic or	other retinopathies, thrombotic	and coagulative disorders,	vascularitis, lymph	angiogenesis, sexual disorders,	age-related macular	degeneration, and treatment	/prevention of endometriosis	and related conditions.	Additional highly preferred	indications include fibromas,	heart disease, cardiac arrest,	heart valve disease, and	vascular disease.	Preferred indications include	blood disorders (e.g., as	described below under	"Immune Activity", "Blood-	Related Disorders", and/or	"Cardiovascular Disorders").
าร	Ā	<u> </u>	<u>.                                    </u>	: IS	11	<u> </u>	<del>p</del>	3 <del>1</del>	<u> </u>	ir	5a	10	al	<u>''</u>		<u>'a</u>	<u> </u>	<u> </u>	a	A	ui	<u>4</u>	h h	3/4	P <sub>1</sub>	ld	p de	[ <del>,,</del> ]	R	<b>)</b>
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Preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below) and immunodeficiencies (e.g., as described below). Additional preferred indications include inflammation and inflammatory disorders (such as acute and chronic inflammatory disorders (e.g., inflammatory diseases, e.g., inflammatory bowel disease and Crohn's disease), and pain management.		Highly preferred indications include allergy, asthma, and rhinitis. Additional preferred indications include infection (e.g., an infectious disease as described below under "Infectious Disease"), and inflammation and inflammation and inflammatory disorders.  Preferred indications also include blood disorders (e.g., as described below under as described below under "Immune Activity", "Blood-
		This reporter assay measures activation of the GATA-3 signaling pathway in HMC-1 human mast cell line. Activation of GATA-3 in mast cells has been linked to cytokine and chemokine production. Assays for the activation of transcription through the GATA3 response element are well-known in the art and may be used or routinely modified to assess
	SEAP in HIB/CRE	Activation of transcription through GATA-3 response element in immune cells (such as mast cells).
	1154	1154
	HFVIC62	HFVIC62
	206	206

		the ah	the ability of nolvnentides of	Related Disorders", and/or
		the in		"Cardiovascular Disorders").
		antibe	antibodies and agonists or	Preferred indications include
		antag	antagonists of the invention) to	autoimmune diseases (e.g.,
		regula		rheumatoid arthritis, systemic
		factor	factors and modulate	lupus erythematosis, multiple
		expre	expression of mast cell genes	sclerosis and/or as described
		lodmi	important for immune response	below) and
		devel	development. Exemplary	immunodeficiencies (e.g., as
	-	assay	assays for transcription	described below). Preferred
		throu	through the GATA3 response	indications include neoplastic
_		eleme	element that may be used or	diseases (e.g., leukemia,
		routir	routinely modified to test	lymphoma, melanoma,
		GAT	GATA3-response element	prostate, breast, lung, colon,
		activi	activity of polypeptides of the	pancreatic, esophageal,
		inven	invention (including antibodies	stomach, brain, liver, and
		anda	and agonists or antagonists of	urinary tract cancers and/or as
	***	the in	the invention) include assays	described below under
		discle	disclosed in Berger et al., Gene	"Hyperproliferative
		66:1-	66:1-10 (1998); Cullen and	Disorders"). Other preferred
		Maln	Malm, Methods in Enzymol	indications include benign
		216:3	216:362-368 (1992); Henthorn	dysproliferative disorders and
		et al.,	et al., Proc Natl Acad Sci USA	pre-neoplastic conditions, such
		85:63	85:6342-6346 (1988); Flavell	as, for example, hyperplasia,
		et al.	et al., Cold Spring Harb Symp	metaplasia, and/or dysplasia.
		Quan	Quant Biol 64:563-571 (1999);	Preferred indications include
		Rodr	Rodriguez-Palmero et al., Eur	anemia, pancytopenia,
		J Imi	J Immunol 29(12):3914-3924	leukopenia, thrombocytopenia,
-		(199	(1999); Zheng and Flavell,	leukemias, Hodgkin's disease,
		Cell		acute lymphocytic anemia
	-	Henc		(ALL), plasmacytomas,

multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, and Lyme Disease.	Highly preferred indications include allergy, asthma, and rhinitis. Additional preferred indications include infection (e.g., an infectious disease as described below under "Infectious Disease"), and inflammation and inflammatory disorders.  Preferred indications also include blood disorders (e.g., as described below under "Immune Activity", "Blood-
contents of each of which are herein incorporated by reference in its entirety. Mast cells that may be used according to these assays are publicly available (e.g., through the ATCC).  Exemplary human mast cells that may be used according to these assays include the HMC-1 cell line, which is an immature human mast cell line established from the peripheral blood of a patient with mast cell leukemia, and exhibits many characteristics of immature mast cells.	This reporter assay measures activation of the NFAT signaling pathway in HMC-1 human mast cell line.  Activation of NFAT in mast cells has been linked to cytokine and chemokine production. Assays for the activation of transcription through the Nuclear Factor of Activated T cells (NFAT) response element are well-known in the art and may be
	Activation of transcription through NFAT response element in immune cells (such as mast cells).
	1154
	HFVIC62
	206

asses the ability of polypepides of the invention invention) to regulate NFAT transcription factors and modulate expression of genes immunonmodulatory functions. Here are according transcription factors and modulate expression of genes immunonmodulatory functions. A searched below). Preferred indications include negative of the impulse element that any be used or routinely prostate, breast, lung, colon, may be used or routinely prostate, breast, lung, colon, pagents of the invention) include assays of disclosed in Berger et al., Fore Natl Acad Sci USA.  10.1929; Henthom 11.1019(1921); Henthom 12.1019(1929); Henthom 12.1019(1929); Henthom 12.1019(1929); Henthom 12.1019(1929); Ali lettred indications include ental., Inframmol and Mafun, Methods in Euzymol 165(12):7212-1236 (1999); Ali lettred indications include ental., Immunol Hutchinson and McCloskey, J. (ALL), plastnaeytomas, according projective and machineson and McCloskey, J. (ALL), plastnaeytomas, according projective and machine an		<del></del>	
used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate NFAT transcription factors and modulate expression of genes involved in immunomodulatory functions. Exemplary assays for transcription through the NFAT response element that may be used or routinely modified to test NFAT- response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Mahn, Methods in Enzymn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); De Boer et al., Int J Biochem Cell Biol 31(10):1221-1236 (1999); Ali et al., J Immunol 165(12):7215-7223 (2000); Hutchinson and McCloskey, J	Related Disorders", and/or "Cardiovascular Disorders"). Preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below) and	described below). Preferred indications include neoplastic diseases (e.g., leukemia, lymphoma, melanoma, prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver, and	
	used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate NFAT transcription factors and modulate expression of genes	immunomodulatory functions. Exemplary assays for transcription through the NFAT response element that may be used or routinely modified to test NFAT-response element activity of	polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); De Boer et al., Int J Biochem Cell Biol 31(10):1221-1236 (1999); Ali et al., J Immunol 165(12):7215-7223 (2000); Hutchinson and McCloskey, J

		16338 (1995), and Turner et al., J Exp Med 188:527-537 (1998), the contents of each of which are herein incorporated by reference in its entirety.  Mast cells that may be used according to these assays are publicly available (e.g., through the ATCC).  Exemplary human mast cells that may be used according to these assays include the HMC-1 cell line, which is an	lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, and Lyme Disease.
HFXAM76	Production of GM-CSF	established from the peripheral blood of a patient with mast cell leukemia, and exhibits many characteristics of immature mast cells.  GM-CSF FMAT. GM-CSF is expressed by activated T cells, macrophages, endothelial cells, and fibroblasts. GM-CSF regulates differentiation and proliferation of granulocytesmacrophage progenitors and enhances antimicrobial activity in neutrophils, monocytes and macrophage. Additionally, GM-CSF plays an important	A highly preferred embodiment of the invention includes a method for stimulating the production of GM-CSF. An alternative highly preferred embodiment of the invention includes a method for inhibiting the production of GM-CSF. Highly preferred indications include inflammation and

role in the differentiation of dendritic cells and monocytes, and increases antigen presentation. GM-CSF is considered to be a inflammatory disorders. An additional highly preferred indication is infection (e.g., as described below under "Infectious Disease".	e. latory re may ffied	agonists or antagonists of the invention) to mediate immunomodulation and inferentiation of leukocytes.  Exemplary assays that test for	رب

	disclosed in Miraglia et al., J	Hodgkin"s lymphoma and
-	Biomolecular Screening 4:193-	Hodgkin"s disease), and/or as
	204 (1999); Rowland et al.,	described below under
	"Lymphocytes: a practical	"Hyperproliferative
	approach" Chapter 6:138-160	Disorders"). Highly preferred
	(2000); and Ye et al., J Leukoc	indications include neoplasms
	Biol (58(2):225-233, the	and cancers, such as, leukemia,
	contents of each of which are	lymphoma, melanoma, and
	herein incorporated by	prostate, breast, lung, colon,
	reference in its entirety.	pancreatic, esophageal,
	Natural killer cells that may be	stomach, brain, liver and
	used according to these assays	urinary cancer. Other preferred
	are publicly available (e.g.,	indications include benign
	through the ATCC) or may be	dysproliferative disorders and
	isolated using techniques	pre-neoplastic conditions, such
	disclosed herein or otherwise	as, for example, hyperplasia,
	known in the art. Natural	metaplasia, and/or dysplasia.
	killer (NK) cells are large	Highly preferred indications
	granular lymphocytes that have	include: suppression of
	cytotoxic activity but do bind	immune reactions to
	antigen. NK cells show	transplanted organs and tissues
	antibody-independent killing	(e.g., bone marrow transplant);
	of tumor cells and also	accelerating myeloid recovery;
	recognize antibody bound on	and mobilizing hematopoietic
	target cells, via NK Fc	progenitor cells. Preferred
	receptors, leading to cell-	indications include boosting a
	mediated cytotoxicity.	T cell-mediated immune
		response, and alternatively,
		suppressing a T cell-mediated
		immune response. Preferred
		indications include anemia,

HFXDJ75	1156	Activation of transcription through AP1 response element in	Assays for the activation of transcription through the AP1 response element are well-known in the art and may be	pancytopenia, leukopenia, thrombocytopenia, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutrophilia, psoriasis, hemophilia, psoriasis, hemophilia, mellitus, endocarditis, meningitis, Lyme Disease, and allergy.  Preferred indications include neoplastic diseases (e.g., as described below under "Hyperproliferative
		immune cells (such as T-cells).	used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to modulate growth and other cell functions.  Exemplary assays for transcription through the AP1 response element that may be used or routinely modified to test AP1-response element activity of polypeptides of the invention (including antibodies	Disorders"), blood disorders (e.g., as described below under "Immune Activity", "Cardiovascular Disorders", and/or "Blood-Related Disorders"), and infection (e.g., an infectious disease as described below under "Infectious Disease"). Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described

and agonists or antagonists of
the invention) include assays
disclosed in Berger et al., Gene
66:1-10 (1988); Cullen and
Malm, Methods in Enzymol
216:362-368 (1992); Henthorn
et al., Proc Natl Acad Sci USA
85:6342-6346 (1988);
Rellahan et al., J Biol Chem
272(49):30806-30811 (1997);
Chang et al., Mol Cell Biol
18(9):4986-4993 (1998); and
Fraser et al., Eur J Immunol
29(3):838-844 (1999), the
contents of each of which are
herein incorporated by
reference in its entirety.
Human T cells that may be
used according to these assays
are publicly available (e.g.,
through the ATCC).
Exemplary human T cells that
may be used according to these
assays include the SUPT cell
line, which is an IL-2 and IL-4
responsive suspension-culture
cell line.

					plasmacytomas, multiple myeloma, Burkitt's lymphoma, granulomatous disease, inflammatory bowel disease, sepsis, psoriasis, suppression of immune reactions to
					transplanted organs and tissues, endocarditis, meningitis, and Lyme Disease.
208	HFXDJ75	1156	Activation of transcription	Assays for the activation of transcription through the CD28	A highly preferred embodiment of the invention
			through CD28	response element are well-	includes a method for
			immune cells (such	used or routinely modified to	An alternative highly preferred
			as T-cells).	assess the ability of	embodiment of the invention
				polypeptides of the invention	includes a method for
				(including antibodies and	inhibiting T cell proliferation.
				agonists or antagonists of the	A highly preferred
				invention) to stimulate IL-2	embodiment of the invention
				expression in T cells.	includes a method for
				Exemplary assays for	activating T cells. An
				transcription through the CD28	alternative highly preferred
				response element that may be	embodiment of the invention
				used or routinely modified to	includes a method for
				test CD28-response element	inhibiting the activation of
				activity of polypeptides of the.	and/or inactivating T cells.
				invention (including antibodies	A highly preferred
···				and agonists or antagonists of	embodiment of the invention
				the invention) include assays	includes a method for
				disclosed in Berger et al., Gene	stimulating (e.g., increasing)
				66:1-10 (1998); Cullen and	IL-2 production. An alternative

highly preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) IL-2 production. Additional highly preferred	indications include inflammation and inflammatory disorders. Highly preferred indications	include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as	described below), immunodeficiencies (e.g., as described below), boosting a T cell-mediated immune		useases (e.g., metanoma, renarcell carcinoma, leukemia, lymphoma, and/or as described below under "Hyperproliferative"	Disorders"). Highly preferred indications include neoplasms and cancers, such as, for example, melanoma (e.g., metastatic melanoma), renal
Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); McGuire and Iacobelli, J	Immunol 159(3):1319-1327 (1997); Parra et al., J Immunol 166(4):2437-2443 (2001); and Butscher et al., J Biol Chem	3(1):552-560 (1998), the contents of each of which are herein incorporated by reference in its entirety. T	cells that may be used according to these assays are publicly available (e.g., through the ATCC).	Exemplary human T cells that may be used according to these assays include the SUPT cell line, which is a suspension	cultule of 1L-2 and 1L-4 responsive T cells.	

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cell carcinoma (e.g., metastatic renal cell carcinoma), leukemia, lymphoma (e.g., T	breast, lung, colon, pancreatic,	liver and urinary cancer. Other	preferred indications include benign dysproliferative	disorders and pre-neoplastic	conditions, such as, for	example, inyperphasia, metaplasia, and/or dysplasia.	A highly preferred indication	includes infection (e.g.,	AIDS, tuberculosis, infections	associated with granulomatous	disease, and osteoporosis,	and/or as described below	under "Infectious Disease"). A	highly preferred indication is	AIDS. Additional highly	preferred indications include	suppression of immune	reactions to transplanted	organs and/or tissues, uveitis,	psoriasis, and tropical spastic	paraparesis. Preferred	indications include blood	disorders (e.g., as described	below under "Immune
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		#-A-8																			<del></del>			
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																								_

Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"). Preferred indications also include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, asthma and allergy.	<b>&gt;</b>
	Activation of transcription through the through NFKB response element in well-known in the art and may immune cells (such as T-cells).  Polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate NFKB transcription factors and modulate expression of immunomedulatory course.
	transcription transcription through NFKB response eleme immune cells (a as T-cells).
	208

multiple sclerosis and/or as described below), and immunodeficiencies (e.g., as described below). An	additional highly preferred indication is infection (e.g., AIDS, and/or an infectious disease as described below	under "Intectious Disease"). Highly preferred indications include neoplastic diseases (e.g., melanoma, leukemia, lymphoma, and/or as described	below under "Hyperproliferative Disorders"). Highly preferred indications include neoplasms	and cancers, such as,melanoma, renal cell carcinoma, leukemia, lymphoma, and prostate, breast, lung, colon, pancreatic,	esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications also
Exemplary assays for transcription through the NFKB response element that may be used or rountinely	modified to test NFKB- response element activity of polypeptides of the invention (including antibodies and	agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol	216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Black et al., Virus Gnes 15(2):105-117	(1997); and Fraser et al., 29(3):838-844 (1999), the contents of each of which are herein incorporated by reference in its entirety. T	according to these assays are publicly available (e.g., through the ATCC).  Exemplary human T cells that may be used according to these assays include the SUPT cell line, which is a suspension culture of IL-2 and IL-4

				responsive T cells.	include anemia, pancytopenia,
				1	leukopenia, thrombocytopenia,
					Hodgkin's disease, acute
					lymphocytic anemia (ALL),
					plasmacytomas, multiple
					myeloma, Burkitt's lymphoma,
					arthritis, AIDS,
	-				granulomatous disease,
					inflammatory bowel disease,
					sepsis, neutropenia,
					neutrophilia, psoriasis,
					hemophilia, hypercoagulation,
					diabetes mellitus, endocarditis,
					meningitis, Lyme Disease,
					suppression of immune
					reactions to transplanted
					organs, asthma and allergy.
	HFXDN63	1157	Activation of	Assays for the activation of	A preferred embodiment of
209		•	transcription	transcription through the	the invention includes a
			through serum	Serum Response Element	method for inhibiting (e.g.,
			response element in	(SRE) are well-known in the	reducing) TNF alpha
			immune cells (such	art and may be used or	production. An alternative
			as natural killer	routinely modified to assess	highly preferred embodiment
			cells).	the ability of polypeptides of	of the invention includes a
				the invention (including	method for stimulating (e.g.,
				antibodies and agonists or	increasing) TNF alpha
				antagonists of the invention) to	production. Preferred
	,			regulate serum response	indications include blood
				factors and modulate the	disorders (e.g., as described
				expression of genes involved	below under "Immune
				in growth and upregulate the	Activity", "Blood-Related

Disorders", and/or	"Cardiovascular Disorders"),	Highly preferred indications	include autoimmune diseases	(e.g., rheumatoid arthritis,	systemic lupus erythematosis,	Crohn"s disease, multiple	sclerosis and/or as described	below), immunodeficiencies	(e.g., as described below),	boosting a T cell-mediated	immune response, and	suppressing a T cell-mediated	immune response. Additional	highly preferred indications	include inflammation and	inflammatory disorders, and	treating joint damage in	patients with rheumatoid	arthritis. An additional highly	preferred indication is sepsis.	Highly preferred indications	include neoplastic diseases	(e.g., leukemia, lymphoma,	and/or as described below	under "Hyperproliferative	Disorders"). Additionally,	highly preferred indications	include neoplasms and	cancers, such as, for example,	leukemia, lymphoma.
function of growth-related	genes in many cell types.	Exemplary assays for	transcription through the SRE	that may be used or routinely	modified to test SRE activity	of the polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) include assays	disclosed in Berger et al., Gene	66:1-10 (1998); Cullen and	Malm, Methods in Enzymol	216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA	85:6342-6346 (1988); Benson	et al., J Immunol 153(9):3862-	3873 (1994); and Black et al.,	Virus Genes 12(2):105-117	(1997), the content of each of	which are herein incorporated	by reference in its entirety. T	cells that may be used	according to these assays are	publicly available (e.g.,	through the ATCC).	Exemplary T cells that may be	used according to these assays	include the NK-YT cell line,	which is a human natural killer	cell line with cytolytic and
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na (e.g., a), solid	tumors, and prostate, breast,	reatic,	iach, bra	liver and urinary cancer. Other	ions incl	erative	-neoplas	as, for	lasia,	or dyspla	ions incl	enia,	nbocyto	e, acute	mia (AL	multiple	t's lymp	granulom	atory bo	nia,	riasis,	ımune	planted	s, hemol	ı, diabete	ditis,	e Disease	on injury	, , , , ,
na, glion nt gliom	and pros	lung, colon, pancreatic,	eal, stom	l urinary	1 indicat	benign dysproliferative	s and pre	ns, such	, hyperp	ia, and/c	d indicat	pancytop	iia, thror	Hodgkin's disease, acute	ytic ane	ytomas,	a, Burkit	AIDS, β	inflamm	neutrope	iilia, pso	ion of in	s to trans	nd tissue	agulation	endocar	tis, Lyme	eperfusi	_ T
melanoma, glioma (e.g., malignant glioma), solid	tumors,	lung, col	esophageal, stomach, brain,	liver and	preferred indications include	benign d	disorders and pre-neoplastic	conditions, such as, for	example, hyperplasia,	metaplasia, and/or dysplasia.	Preferred indications include	anemia, pancytopenia,	leukopenia, thrombocytopenia,	Hodgkin	lymphocytic anemia (ALL),	plasmacytomas, multiple	myeloma, Burkitt's lymphoma,	arthritis, AIDS, granulomatous	disease, inflammatory bowel	disease, neutropenia,	neutrophilia, psoriasis,	suppression of immune	reactions to transplanted	organs and tissues, hemophilia,	hypercoagulation, diabetes	mellitus, endocarditis,	meningitis, Lyme Disease,	cardiac reperfusion injury, and	
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cytotoxic activity.																													
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additional preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease").	ay d d d d 1. 1. 1. 1. 1. 1. 1. 1. 1. 1. 1. 1. 1.
addition is infect disease under "I	nay ed he
	Production of ICAM-1
	1158
	HFXGT26
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			include microvascular endothelial cells (MVEC).	
	1159	Production of TNF	TNFa FMAT. Assays for	A highly preferred
		alpha by dendritic	immunomodulatory proteins	embodiment of the invention
		CIIIS	produced by activated macrophages. T cells	includes a method for
			fibroblasts, smooth muscle,	TNF alpha production. An
			and other cell types that exert a	alternative highly preferred
			wide variety of inflammatory	embodiment of the invention
			and cytotoxic effects on a	includes a method for
			variety of cells are well known	stimulating (e.g., increasing)
			in the art and may be used or	TNF alpha production.
_			routinely modified to assess	Highly preferred indications
			the ability of polypeptides of	include blood disorders (e.g.,
			the invention (including	as described below under
			antibodies and agonists or	"Immune Activity", "Blood-
			antagonists of the invention) to	Related Disorders", and/or
			mediate immunomodulation,	"Cardiovascular Disorders"),
			modulate inflammation and	Highly preferred indications
			cytotoxicity. Exemplary	include autoimmune diseases
			assays that test for	(e.g., rheumatoid arthritis,
			immunomodulatory proteins	systemic lupus erythematosis,
			evaluate the production of	Crohn"s disease, multiple
			cytokines such as tumor	sclerosis and/or as described
			necrosis factor alpha (TNFa),	below), immunodeficiencies
			and the induction or inhibition	(e.g., as described below),
			of an inflammatory or	boosting a T cell-mediated
		-	cytotoxic response. Such	immune response, and
			assays that may be used or	suppressing a T cell-mediated
			routinely modified to test	immune response. Additional
_			immunomodulatory activity of	highly preferred indications

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on and	inflammatory disorders, and	ge in	natoid	arthritis. An additional highly	preferred indication is sepsis.	Highly preferred indications	include neoplastic diseases	(e.g., leukemia, lymphoma,	below	erative	Disorders"). Additionally,	highly preferred indications	and	cancers, such as, leukemia,	lymphoma, melanoma, glioma	(e.g., malignant glioma), solid	tumors, and prostate, breast,	atic,	esophageal, stomach, brain,	liver and urinary cancer. Other	preferred indications include	tive	disorders and pre-neoplastic	for	ia,	metaplasia, and/or dysplasia.	Preferred indications include	nia,	leukopenia, thrombocytopenia,	atito
ımmatic	y disor	t damag	n rheum	n additio	dication	erred in	plastic c	nia, lyn	scribed	erprolif	Addit	rred inc	slasms a	h as, le	melano	nant glic	prostat	pancre	stomac	nary ca	dication	rolifera	d pre-n	such as,	perplas	and/or o	dicatior	cytoper	thromb	900001
include inflammation and	ımmatoı	treating joint damage in	patients with rheumatoid	itis. An	erred in	aly prefe	ide neoj	, leuker	and/or as described below	under "Hyperproliferative	rders")	ly prefe	include neoplasms and	ers, suc	shoma,	, maligi	ors, and	lung, colon, pancreatic,	hageal,	and uri	erred in	benign dysproliferative	rders an	conditions, such as, for	example, hyperplasia,	ıplasia,	erred in	anemia, pancytopenia,	openia,	Hodokin's disease acute
inch	infla	treat	patie	arth			inch	(e.g.	and/	pun	Disc	high	inch	canc	lyml	(e.g.	_	lung			prefe	beni	diso	conc	exan	meta	Pref	aner	leuk	Hod
ention	ъ	of the	ys	al., J	3 4:193	al.,	cal	8-160	., Eur J	3890		3593	т,:	3.	al., J	∞	each of	orated	ety.	hat may	ese	using	rein or	art.	ıre	in	ch,	en	e and	aration
the inve	odies a	gonists	de assa	aglia et	reening	land et	a practi	ter 6:13	elt et al	.3886-	et al., J	:3585-	elt et al	19-292	delli et	822-82	ents of	incorp	ts entir	c cells t	ng to the	solated	osed he	n in the	c cells a	ng cells	ıre, whi	by antig	s, initiat	1 nrolify
ides of	ng antib	or antag	n) inclu	d in Mir	cular So	9); Row	ocytes:	า" Chap	Verhass	1 28(11)	<b>Jahlen</b>	1160(7)	Verhass	1158:29	and Nar	<b>Biol</b> 65:	he cont	e hereir	nce in i	lendriti	accordin	ay be is	es discl	e know	lendriti	resenti	on cultı	livated 1	ytokines	unregulate T cell proliferation
polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include assays	disclosed in Miraglia et al., J	Biomolecular Screening 4:193-	204(1999); Rowland et al.,	"Lymphocytes: a practical	approach" Chapter 6:138-160	(2000); Verhasselt et al., Eur J	Immunol 28(11):3886-3890	(1198); Dahlen et al., J	Immunol 160(7):3585-3593	(1998); Verhasselt et al., J	Immunol 158:2919-2925	(1997); and Nardelli et al., J	Leukoc Biol 65:822-828	(1999), the contents of each of	which are herein incorporated	by reference in its entirety.	Human dendritic cells that may	be used according to these	assays may be isolated using	techniques disclosed herein or	otherwise known in the art.	Human dendritic cells are	antigen presenting cells in	suspension culture, which,	when activated by antigen	and/or cytokines, initiate and	nreomia
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of the invention includes a	method for stimulating	adipocyte differentiation. An	alternative highly preferred	embodiment of the invention	includes a method for	inhibiting adipocyte	differentiation. A highly	preferred embodiment of the	invention includes a method	for stimulating (e.g.,	increasing) adipocyte	activation. An alternative	highly preferred embodiment	of the invention includes a	method for inhibiting the	activation of (e.g., decreasing)	and/or inactivating adipocytes.	Highly preferred indications	include endocrine disorders	(e.g., as described below under	"Endocrine Disorders").	Highly preferred indications	also include neoplastic	diseases (e.g., lipomas,	liposarcomas, and/or as	described below under	"Hyperproliferative	Disorders"). Preferred	indications include blood	11
and agonists or antagonists of	the invention) to promote or	inhibit cell proliferation,	activation, and differentiation.	Exemplary assays for ERK	kinase activity that may be	used or routinely modified to	test ERK kinase-induced	activity of polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) include the	assays disclosed in Forrer et	al., Biol Chem 379(8-9):1101-	1110 (1998); Le Marchand-	Brustel Y, Exp Clin	Endocrinol Diabetes	107(2):126-132 (1999);	Kyriakis JM, Biochem Soc	Symp 64:29-48 (1999); Chang	and Karin, Nature	410(6824):37-40 (2001); and	Cobb MH, Prog Biophys Mol	Biol 71(3-4):479-500 (1999);	the contents of each of which	are herein incorporated by	reference in its entirety.	Mouse adipocyte cells that	may be used according to these	assays are publicly available	(DDT A sht do county of a
1111						a de la companya de l																								
				16-																										

congestive heart failure, blood vessel blockage, heart disease, stroke, impotence and/or as described below under	"Cardiovascular Disorders", and/or "Blood-Related Disorders"), immune disorders (e.g., as described below under	disorders (e.g., as described below under "Neural Activity and Neurological Diseases"), and infection (e.g., as described below under	"Infectious Disease"). A highly preferred indication is diabetes mellitus. An additional highly preferred indication is a complication associated with diabetes (e.g.,	diabetic retinopathy, diabetic nephropathy, kidney disease (e.g., renal failure, nephropathy and/or other diseases and disorders as	described in the "Renal Disorders" section below), diabetic neuropathy, nerve disease and nerve damage (e.g., due to diabetic
Exemplary mouse adipocyte cells that may be used according to these assays include 3T3-L1 cells. 3T3-L1 is an adherent mouse	preadipocyte cell line that is a continuous substrain of 3T3 fibroblast cells developed through clonal isolation and	adipose-like conversion under appropriate differentiation conditions known in the art.			
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neuropathy), blood vessel	blockage, heart disease, stroke,	impotence (e.g., due to diabetic	neuropathy or blood vessel	blockage), seizures, mental	confusion, drowsiness,	nonketotic hyperglycemic-	hyperosmolar coma,	cardiovascular disease (e.g.,	heart disease, atherosclerosis,	microvascular disease,	hypertension, stroke, and other	diseases and disorders as	described in the	"Cardiovascular Disorders"	section below), dyslipidemia,	endocrine disorders (as	described in the "Endocrine	Disorders" section below),	neuropathy, vision impairment	(e.g., diabetic retinopathy and	blindness), ulcers and impaired	wound healing, infection (e.g.,	infectious diseases and	disorders as described in the	"Infectious Diseases" section	below (particularly of the	urinary tract and skin). An	additional highly preferred	indication is obesity and/or	with his accountations accountated with
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obesity. Additional highly preferred indications include weight loss or alternatively, weight gain. Additional	highly preferred indications are complications associated with insulin resistance.  Additional highly preferred indications are disorders of the	musculoskeletal systems including myopathies, muscular dystrophy, and/or as described herein.  Additional highly preferred	indications include, hypertension, coronary artery disease, dyslipidemia, gallstones, osteoarthritis, degenerative arthritis, eating disorders, fibrosis, cachexia,	and kidney diseases or disorders. Preferred indications include neoplasms and cancer, such as, lymphoma, leukemia and breast, colon, and kidney.	cancer. Additional preferred indications include melanoma, prostate, lung, pancreatic, esophageal, stomach, brain, liver, and urinary cancer.

Highly preferred indications include lipomas and liposarcomas. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia.	IgG in Human B cells IgG in Human B cells SAC	
	IgG in Human B cells IgG in Human B cells SAC	
	1161	1162
	HFXHK73 HFXKJ03	HFXKJ03
	213	214

				Table 1	
				colon cancer. See, Patan et al.,	
				Circ Res, 89(8):732-39 (2001),	
				the contents of which are	
				herein incorporated by	
				reference in its entirety.	
,	HFXKJ03	1162	Activation of	Assays for the activation of	A preferred embodiment of
214			transcription	transcription through the	the invention includes a
			through serum	Serum Response Element	method for inhibiting (e.g.,
			response element in	(SRE) are well-known in the	reducing) TNF alpha
			immune cells (such	art and may be used or	production. An alternative
			as natural killer	routinely modified to assess	highly preferred embodiment
			cells).	the ability of polypeptides of	of the invention includes a
				the invention (including	method for stimulating (e.g.,
				antibodies and agonists or	increasing) TNF alpha
				antagonists of the invention) to	production. Preferred
				regulate serum response	indications include blood
				factors and modulate the	disorders (e.g., as described
				expression of genes involved	below under "Immune
				in growth and upregulate the	Activity", "Blood-Related
	·			function of growth-related	Disorders", and/or
,				genes in many cell types.	"Cardiovascular Disorders"),
				Exemplary assays for	Highly preferred indications
-				transcription through the SRE	include autoimmune diseases
				that may be used or routinely	(e.g., rheumatoid arthritis,
				modified to test SRE activity	systemic lupus erythematosis,
				of the polypeptides of the	Crohn"s disease, multiple
				invention (including antibodies	sclerosis and/or as described
				and agonists or antagonists of	below), immunodeficiencies
				the invention) include assays	(e.g., as described below),
				disclosed in Berger et al., Gene	boosting a T cell-mediated
				66:1-10 (1998); Cullen and	immune response, and

	Malm, Methods in Enzymol	suppressing a T cell-mediated
	216:362-368 (1992); Henthorn	immune response. Additional
	et al., Proc Natl Acad Sci USA	highly preferred indications
	85:6342-6346 (1988); Benson	include inflammation and
	et al., J Immunol 153(9):3862-	inflammatory disorders, and
	3873 (1994); and Black et al.,	treating joint damage in
	Virus Genes 12(2):105-117	patients with rheumatoid
	(1997), the content of each of	arthritis. An additional highly
	which are herein incorporated	preferred indication is sepsis.
	by reference in its entirety. T	Highly preferred indications
	cells that may be used	include neoplastic diseases
-	according to these assays are	(e.g., leukemia, lymphoma,
	publicly available (e.g.,	and/or as described below
	through the ATCC).	under "Hyperproliferative
	Exemplary T cells that may be	Disorders"). Additionally,
	used according to these assays	highly preferred indications
	include the NK-YT cell line,	include neoplasms and
	which is a human natural killer	cancers, such as, for example,
	cell line with cytolytic and	leukemia, lymphoma,
	cytotoxic activity.	melanoma, glioma (e.g.,
		malignant glioma), solid
		tumors, and prostate, breast,
		lung, colon, pancreatic,
		esophageal, stomach, brain,
		liver and urinary cancer. Other
		preferred indications include
		benign dysproliferative
		disorders and pre-neoplastic
		conditions, such as, for
		example, hyperplasia,
		metaplasia, and/or dysplasia.

					Preferred indications include
					anemia, pancytopenia,
					leukopenia, thrombocytopenia,
					Hodgkin's disease, acute
					lymphocytic anemia (ALL),
					plasmacytomas, multiple
_					myeloma, Burkitt's lymphoma,
					arthritis, AIDS, granulomatous
					disease, inflammatory bowel
					disease, neutropenia,
					neutrophilia, psoriasis,
					suppression of immune
· · ·					reactions to transplanted
					organs and tissues, hemophilia,
					hypercoagulation, diabetes
					mellitus, endocarditis,
					meningitis, Lyme Disease,
					cardiac reperfusion injury, and
					asthma and allergy. An
					additional preferred indication
					is infection (e.g., an infectious
					disease as described below
					under "Infectious Disease").
!	HFXKT05	1163	Myoblast cell	Assays for muscle cell	Highly preferred indications
215	,		proliferation	proliferation are well known in	include diabetes, myopathy,
				the art and may be used or	muscle cell atrophy, cancers of
				routinely modified to assess	muscle (such as,
				the ability of polypeptides of	rhabdomyoma, and
				the invention (including	rhabdosarcoma),
				antibodies and agonists or	cardiovascular disorders (such
		į	70.00	antagonists of the invention) to	as congestive heart failure,

cachexia, myxomas, fibromas, congenital cardiovascular abnormalities, heart disease, cardiac arrest, heart valve disease, vascular disease, and	also as described below under "Cardiovascular Disorders"), stimulating myoblast proliferation, and inhibiting	myoblast proliteration.					
stimulate or inhibit myoblast cell proliferation. Exemplary assays for myoblast cell proliferation that may be used or routinely modified to test	activity of polypeptides and antibodies of the invention (including agonists or antagonists of the invention)	include, for example, assays disclosed in: Soeta, C., et al. "Possible role for the c-ski gene in the proliferation of	myogenic cells in regenerating skeletal muscles of rats" Dev Growth Differ Apr;43(2):155-	o4 (2001); Ewton DZ, et al., "IGF binding proteins-4, -5 and -6 may play specialized roles during L6 myoblast proliferation and	differentiation" J Endocrinol Mar;144(3):539-53 (1995); and, Pampusch MS, et	growth factor beta on proliferation of L6 and embryonic porcine myogenic	cells" J Cell Physiol Jun;143(3):524-8 (1990); the contents of each of which are

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herein incorporated by reference in their entirety.  Exemplary myoblast cells that may be used according to these assays include the rat myoblast L6 cell line. Rat myoblast L6 cells are an adherent rat myoblast cell line, isolated from primary cultures of rat thigh muscle, that fuse to form multinucleated myotubes and striated fibers after culture in differentiation media.	Kinase assay. Kinase assays, for example an Elk-1 kinase assay, for ERK signal transduction that regulate cell proliferation or differentiation are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote or inhibit cell proliferation, activation, and differentiation. Exemplary assays for ERK kinase activity that may be used or routinely modified to	test ERK kinase-induced
	Activation of Adipocyte ERK Signaling Pathway	
j	1164	
	HFXKY27	
	216	

preferred embodiment of the invention includes a method for stimulating (e.g., increasing) adipocyte activation. An alternative highly preferred embodiment of the invention includes a	activation of (e.g., decreasing) and/or inactivating adipocytes. Highly preferred indications include endocrine disorders (e.g., as described below under "Endocrine Disorders"). Highly preferred indications	also include neoplastic diseases (e.g., lipomas, liposarcomas, and/or as described below under "Hyperproliferative Disorders"). Preferred indications include blood disorders (e.g., hypertension, congestive heart failure, blood vessel blockage, heart disease,	stroke, impotence and/or as described below under "Immune Activity", "Cardiovascular Disorders", and/or "Blood-Related Disorders", immune disorders
activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include the assays disclosed in Forrer et al., Biol Chem 379(8-9):1101-1110 (1998); Le Marchand-Brustol V. Ever Clin	Endocrinol Diabetes 107(2):126-132 (1999); Kyriakis JM, Biochem Soc Symp 64:29-48 (1999); Chang and Karin, Nature 410(6824):37-40 (2001); and Cobb MH, Prog Biophys Mol	Biol 71(3-4):479-500 (1999); the contents of each of which are herein incorporated by reference in its entirety.  Mouse adipocyte cells that may be used according to these assays are publicly available (e.g., through the ATCC).  Exemplary mouse adipocyte cells that may be used	according to these assays include 3T3-L1 cells. 3T3-L1 is an adherent mouse preadipocyte cell line that is a continuous substrain of 3T3 fibroblast cells developed

		through clonal isolation and	(e.g., as described below under
		undergo a pre-adipocyte to	"Immune Activity"), neural
		adipose-like conversion under	disorders (e.g., as described
		appropriate differentiation	below under "Neural Activity
		conditions known in the art.	and Neurological Diseases"),
			and infection (e.g., as
••			described below under
			"Infectious Disease").
			A highly preferred indication
			is diabetes mellitus. An
			additional highly preferred
-			indication is a complication
			associated with diabetes (e.g.,
			diabetic retinopathy, diabetic
			nephropathy, kidney disease
			(e.g., renal failure,
	all or see Park		nephropathy and/or other
			diseases and disorders as
			described in the "Renal
			Disorders" section below),
			diabetic neuropathy, nerve
-			disease and nerve damage
			(e.g., due to diabetic
			neuropathy), blood vessel
			blockage, heart disease, stroke,
			impotence (e.g., due to diabetic
			neuropathy or blood vessel
			blockage), seizures, mental
			confusion, drowsiness,
			nonketotic hyperglycemic-
			hyperosmolar coma,

cardiovascular disease (e.g.,	microvascular disease	hypertension, stroke, and other	diseases and disorders as	described in the	"Cardiovascular Disorders"	section below), dyslipidemia,	endocrine disorders (as	described in the "Endocrine	Disorders" section below),	neuropathy, vision impairment	(e.g., diabetic retinopathy and	blindness), ulcers and impaired	wound healing, infection (e.g.,	infectious diseases and	disorders as described in the	"Infectious Diseases" section	below (particularly of the	urinary tract and skin). An	additional highly preferred	indication is obesity and/or	complications associated with	obesity. Additional highly	preferred indications include	weight loss or alternatively,	weight gain. Additional	highly preferred indications are	complications associated with	insulin resistance.	Additional highly preferred
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								-																					

indications are disorders of the musculoskeletal systems including myopathies, muscular dystrophy, and/or as described herein.  Additional highly preferred	indications include, hypertension, coronary artery disease, dyslipidemia, gallstones, osteoarthritis, degenerative arthritis, eating	disorders, fibrosis, cachexia, and kidney diseases or disorders. Preferred indications include neoplasms and cancer, such as, lymphoma, leukemia and breast, colon, and kidney cancer. Additional preferred	indications include melanoma, prostate, lung, pancreatic, esophageal, stomach, brain, liver, and urinary cancer. Highly preferred indications include lipomas and liposarcomas. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia.

	HFXKY27	1164	Activation of	Assays for the activation of	Highly preferred indications
216			transcription	transcription through the	include neoplastic diseases
			through GAS	Gamma Interferon Activation	(e.g., leukemia, lymphoma,
			response element in	Site (GAS) response element	and/or as described below
			immune cells (such	are well-known in the art and	under "Hyperproliferative
			as T-cells).	may be used or routinely	Disorders"). Highly preferred
				modified to assess the ability	indications include neoplasms
				of polypeptides of the	and cancers, such as, for
				invention (including antibodies	example, leukemia, lymphoma
				and agonists or antagonists of	(e.g., T cell lymphoma,
				the invention) to regulate	Burkitt's lymphoma, non-
		-11		STAT transcription factors and	Hodgkins lymphoma,
				modulate gene expression	Hodgkin"s disease),
	*****			involved in a wide variety of	melanoma, and prostate,
				cell functions. Exemplary	breast, lung, colon, pancreatic,
1.4				assays for transcription	esophageal, stomach, brain,
				through the GAS response	liver and urinary cancer. Other
				element that may be used or	preferred indications include
				routinely modified to test	benign dysproliferative
				GAS-response element activity	disorders and pre-neoplastic
				of polypeptides of the	conditions, such as, for
				invention (including antibodies	example, hyperplasia,
				and agonists or antagonists of	metaplasia, and/or dysplasia.
				the invention) include assays	Preferred indications include
				disclosed in Berger et al., Gene	autoimmune diseases (e.g.,
				66:1-10 (1998); Cullen and	rheumatoid arthritis, systemic
				Malm, Methods in Enzymol	lupus erythematosis, multiple
				216:362-368 (1992); Henthorn	sclerosis and/or as described
				et al., Proc Natl Acad Sci USA	below), immunodeficiencies
				85:6342-6346 (1988);	(e.g., as described below),
				Matikainen et al., Blood	boosting a T cell-mediated

immune response, and suppressing a T cell-mediated immune response. Additional preferred indications include inflammation and	inflammatory disorders. Highly preferred indications include blood disorders (e.g., as described below under	"Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"), and infection (e.g., viral	infections, tuberculosis, infections associated with chronic granulomatosus disease and malignant	osteoporosis, and/or an infectious disease as described below under "Infectious Disease"). An additional preferred indication is idiopathic pulmonary fibrosis.	Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease,
93(6):1980-1991 (1999); and Henttinen et al., J Immunol 155(10):4582-4587 (1995), the contents of each of which are herein incorporated by	reference in its entirety.  Exemplary mouse T cells that may be used according to these assays are publicly available	(e.g., through the ATCC). Exemplary T cells that may be used according to these assays include the CTLL cell line,	which is a suspension culture of IL-2 dependent cytotoxic T cells.		

sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, and asthma and allergy.			Preferred embodiments of the invention include using polypeptides of the invention (or antibodies, agonists, or antagonists thereof) in detection, diagnosis, prevention, and/or treatment of Vascular Disease, Atherosclerosis, Restenosis, Stroke, and Asthma.
			Assays for measuring expression of ICAM-1 are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate ICAM-1 expression. Exemplary assays that may be used or routinely modified to measure ICAM-1 expression include assays disclosed in: Rolfe BE, et al., Atherosclerosis, 149(1):99-110 (2000); Panettieri RA Jr, et al., J Immunol, 154(5):2358-2365 (1995); and, Grunstein MM, et
	Glucose Production in H4IIE	IgG in Human B cells	Production of ICAM-1
	1164	1164	1165
	HFXKY27	HFXKY27	HGBFO79
	216	216	217

al., Am J Physiol Lung Cell Mol Physiol, 278(6):L1154- L1163 (2000), the contents of each of which is herein incorporated by reference in its entirety. Cells that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary cells that may be used according to these assays include Aortic Smooth Muscle Cells (AOSMC); such as bovine AOSMC.	immune cells (such increases or decreases) of include asthma, allergy, as the HMC-1 cells in vitro are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention of eosinophil cells immunological disorders (e.g., and cell lines. For example, and ecll lines. For example, including as described below under the CellTiter-Gloô  Highly preferred indications include asthma, allergy, mast cells, mastocytosis (a rare, human mast cell surface and proliferation of mast cells, and their proliferation and action in the skin, central antibodies and agonists or nervous system, and other and cell lines. For example, "Immune Activity", and "Im
	1165
	HGBFO79
	217

Madison, WI, USA ) can be below under "Infectious used to measure the number of viable cells in culture based on quantitation of the ATP below under "Infectious diseases", autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus		immunoglobulin E -antigen, promoted by T helper cell type 2 cytokines) is an important component of allergic disease. Dysregulation of mast cell apoptosis may play a role in allergic disease and mast cell	tumor survival. Mast cell lines that may be used according to these assays are publicly available and/or may be routinely generated.  Exemplary mast cells that may be used according to these	assays include HMC-1, which is an immature human mast cell line established from the peripheral blood of a patient with mast cell leukemia, and exhibits many characteristics
N w iv	pi p			

construct bry and coding luene rst specific tolesterol lway. See Siol. Chem. 41(993), the h are herein reference in its vere treated atants, and as measured lepG2 is a llular ne (ATCC Knowles et al., 7-9 (1980), the h are herein reference in its		tivation of Highly preferred indications ough the include blood disorders (e.g., as described below under 'Immune Activity', "Bloodin the art and Related Disorders', and/or "Cardiovascular Disorders").
Reporter Assay: construct contains regulatory and coding sequence of squalene synthetase, the first specific enzyme in the cholesterol biosynthetic pathway. See Jiang, et al., J. Biol. Chem. 268:12818-128241(993), the contents of which are herein incorporated by reference in its entirety. Cells were treated with SID supernatants, and SEAP activity was measured after 72 hours. HepG2 is a human hepatocellular carcinoma cell line (ATCC HB-8065). See Knowles et al., Science. 209:497-9 (1980), the contents of which are herein incorporated by reference in its entirety.		Assays for the activation of transcription through the Nuclear Factor of Activated T cells (NFAT) response element are well-known in the art and may be used or routinely modified to assess the ability of polyneptides of the
Inhibition of squalene synthetase gene transcription.	CD71 in Human T cells	Activation of transcription through NFAT response element in immune cells (such as natural killer cells).
1166	1166	1167
HGBHE57	HGBHE57	HGBIB74
218	218	219

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-	immunodeficiencies (e.g., as described below), boosting a T cell-mediated immune	response, and suppressing a T cell-mediated immune response. Additional highly preferred indications include	inflammation and inflammatory disorders. An additional highly preferred indication is infection (e.g., an	intectious disease as described below under "Infectious Disease"). Preferred indications include neoplastic diseases (e.g., leukemia,	lymphoma, and/or as described below under "Hyperproliferative Disorders"). Preferred indications include neoplasms	and cancers, such as, for example, leukemia, lymphoma, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred
S D	modulate expression of genes involved in immunomodulatory functions.	Exemplary assays for transcription through the NFAT response element that may be used or routinely	modified to test NFAT- response element activity of polypeptides of the invention (including antibodies and	agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol	216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Aramburu et al., J Exp Med 182(3):801-810 (1995); De	Boer et al., Int J Biochem Cell Biol 31(10):1221-1236 (1999); Fraser et al., Eur J Immunol 29(3):838-844 (1999); and Yeseen et al., J Biol Chem 268(19):14285-14293 (1993),

				the contents of each of which	indications include benign
				are herein incorporated by	dysproliferative disorders and
				reference in its entirety. NK	pre-neoplastic conditions, such
				cells that may be used	as, for example, hyperplasia,
				according to these assays are	metaplasia, and/or dysplasia.
				publicly available (e.g.,	Preferred indications also
				through the ATCC).	include anemia, pancytopenia,
				Exemplary human NK cells	leukopenia, thrombocytopenia,
				that may be used according to	Hodgkin's disease, acute
				these assays include the NK-	lymphocytic anemia (ALL),
				YT cell line, which is a human	plasmacytomas, multiple
				natural killer cell line with	myeloma, Burkitt's lymphoma,
				cytolytic and cytotoxic	arthritis, AIDS, granulomatous
				activity.	disease, inflammatory bowel
					disease, sepsis, neutropenia,
					neutrophilia, psoriasis,
					suppression of immune
					reactions to transplanted
					organs and tissues,
					hemophilia, hypercoagulation,
					diabetes mellitus, endocarditis,
					meningitis, Lyme Disease,
					asthma and allergy.
,	HGBIB74	1167	Activation of	Assays for the activation of	A preferred embodiment of
219			transcription	transcription through the	the invention includes a
			through serum	Serum Response Element	method for inhibiting (e.g.,
			response element in	(SRE) are well-known in the	reducing) TNF alpha
			immune cells (such	art and may be used or	production. An alternative
			as natural killer	routinely modified to assess	highly preferred embodiment
			cells).	the ability of polypeptides of	of the invention includes a
				the invention (including	method for stimulating (e.g.,

	10	antibodies and agonists or	increasing) TME alaba
			incleasing) in an pina
	<u>ar</u>	antagonists of the invention) to	production. Preferred
	re	regulate serum response	indications include blood
	fa fa	factors and modulate the	disorders (e.g., as described
	<u> </u>	expression of genes involved	below under "Immune
		in growth and upregulate the	Activity", "Blood-Related
	nj	function of growth-related	Disorders", and/or
		genes in many cell types.	"Cardiovascular Disorders"),
	<u>一</u>	Exemplary assays for	Highly preferred indications
	<u> </u>	transcription through the SRE	include autoimmune diseases
	th	that may be used or routinely	(e.g., rheumatoid arthritis,
	ш	modified to test SRE activity	systemic lupus erythematosis,
	to	of the polypeptides of the	Crohn"s disease, multiple
	ni	invention (including antibodies	sclerosis and/or as described
	ar	and agonists or antagonists of	below), immunodeficiencies
	th	the invention) include assays	(e.g., as described below),
	- di	disclosed in Berger et al., Gene	boosting a T cell-mediated
	99	66:1-10 (1998); Cullen and	immune response, and
	<u> </u>	Malm, Methods in Enzymol	suppressing a T cell-mediated
	21	216:362-368 (1992); Henthorn	immune response. Additional
	et	et al., Proc Natl Acad Sci USA	highly preferred indications
	788	85:6342-6346 (1988); Benson	include inflammation and
	et	et al., J Immunol 153(9):3862-	inflammatory disorders, and
	<u>38</u>	3873 (1994); and Black et al.,	treating joint damage in
	<u> </u>	Virus Genes 12(2):105-117	patients with rheumatoid
	(1)	(1997), the content of each of	arthritis. An additional highly
	M	which are herein incorporated	preferred indication is sepsis.
		by reference in its entirety. T	Highly preferred indications
	93	cells that may be used	include neoplastic diseases
e de la constantina della cons	ac	according to these assays are	(e.g., leukemia, lymphoma,
	านี	publicly available (e.g.,	and/or as described below

under "Hyperproliferative Disorders"). Additionally, highly preferred indications include neoplasms and cancers, such as, for example, leukemia, lymphoma, melanoma, glioma (e.g.,	malignant glioma), solid tumors, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benion dysproliferative	disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include anemia, pancytopenia, thrombocytopenia	Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted
through the ATCC). Exemplary T cells that may be used according to these assays include the NK-YT cell line, which is a human natural killer cell line with cytolytic and cytotoxic activity.			
			,

organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, cardiac reperfusion injury, and asthma and allergy. An additional preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease").		Highly preferred indications include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Highly preferred indications include neoplasms and cancers, such as, for example, leukemia, lymphoma (e.g., T cell lymphoma, non-Hodgkins lymphoma, non-Hodgkin's disease), melanoma, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative
		Assays for the activation of transcription through the Gamma Interferon Activation Site (GAS) response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate STAT transcription factors and modulate gene expression involved in a wide variety of cell functions. Exemplary assays for transcription through the GAS response element that may be used or routinely modified to test
	SEAP in NK16/STAT6	Activation of transcription through GAS response element in immune cells (such as T-cells).
	1167	1167
	HGBIB74	HGBIB74
	219	219

disorders and pre-neoplastic conditions, such as, for example, hyperplasia,	metaplasia, and/or dysplasia. Preferred indications include	rheumatoid arthritis, systemic	lupus erythematosis, multiple sclerosis and/or as described	below), immunodeficiencies	(e.g., as described below), boosting a T cell-mediated	immune response, and	suppressing a T cell-mediated	immune response. Additional	preferred indications include	inflammation and	inflammatory disorders.	Highly preferred indications	include blood disorders (e.g.,	as described below under	"Immune Activity", "Blood-	Related Disorders", and/or	"Cardiovascular Disorders"),	and infection (e.g., viral	infections, tuberculosis,	infections associated with	chronic granulomatosus	disease and malignant	osteoporosis, and/or an	infectious disease as described
GAS-response element activity of polypeptides of the invention (including antibodies	and agonists or antagonists of the invention) include assays	66:1-10 (1998); Cullen and	Malm, Methods in Enzymol 216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA	85:6342-6346 (1988); Matikainen et al., Blood	93(6):1980-1991 (1999); and	Henttinen et al., J Immunol	155(10):4582-4587 (1995), the	contents of each of which are	herein incorporated by	reference in its entirety.	Exemplary human T cells,	such as the SUPT cell line, that	may be used according to these	assays are publicly available	(e.g., through the ATCC).								
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below under "Infectious Disease"). An additional preferred indication is idiopathic pulmonary fibrosis. Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, and asthma and allergy.	A preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) TNF alpha production. An alternative preferred embodiment of the invention includes a method for stimulating (e.g., increasing) TNF alpha production. Preferred
	Assays for the activation of transcription through the Serum Response Element (SRE) are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to
	Activation of transcription through serum response element in immune cells (such as T-cells).
	1168
	HGLAL82
	220

	regulate the serum response	indications include blood
	factors and modulate the	disorders (e.g., as described
	expression of genes involved	below under "Immune
	in growth. Exemplary assays	Activity", "Blood-Related
	for transcription through the	Disorders", and/or
	SRE that may be used or	"Cardiovascular Disorders"),
	routinely modified to test SRE	Highly preferred indications
	activity of the polypeptides of	include autoimmune diseases
	the invention (including	(e.g., rheumatoid arthritis,
	antibodies and agonists or	systemic lupus erythematosis,
	antagonists of the invention)	Crohn's disease, multiple
	include assays disclosed in	sclerosis and/or as described
	Berger et al., Gene 66:1-10	below), immunodeficiencies
•	(1998); Cullen and Malm,	(e.g., as described below),
	Methods in Enzymol 216:362-	boosting a T cell-mediated
	368 (1992); Henthorn et al.,	immune response, and
	Proc Natl Acad Sci USA	suppressing a T cell-mediated
	85:6342-6346 (1988); and	immune response. Additional
	Black et al., Virus Genes	highly preferred indications
	12(2):105-117 (1997), the	include inflammation and
	content of each of which are	inflammatory disorders, and
	herein incorporated by	treating joint damage in
	reference in its entirety. T	patients with rheumatoid
	cells that may be used	arthritis. An additional highly
	according to these assays are	preferred indication is sepsis.
	publicly available (e.g.,	Highly preferred indications
	through the ATCC).	include neoplastic diseases
	Exemplary mouse T cells that	(e.g., leukemia, lymphoma,
	may be used according to these	and/or as described below
	assays include the CTLL cell	under "Hyperproliferative
	line, which is an IL-2	Disorders"). Additionally,

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highly preferred indications include neoplasms and cancers, such as, for example,	leukemia, lymphoma, melanoma, glioma (e.g.,	malignant glioma), solid	tumors, and prostate, breast,	esophageal, stomach, brain,	liver and urinary cancer. Other	preferred indications include	benign dysproliferative	disorders and pre-neoplastic	conditions, such as, for	example, hyperplasia,	metaplasia, and/or dysplasia.	Preferred indications include	anemia, pancytopenia,	leukopenia, thrombocytopenia,	Hodgkin's disease, acute	lymphocytic anemia (ALL),	plasmacytomas, multiple	myeloma, Burkitt's lymphoma,	arthritis, AIDS, granulomatous	disease, inflammatory bowel	disease, neutropenia,	neutrophilia, psoriasis,	suppression of immune	reactions to transplanted	organs and tissues,	hemophilia, hypercoagulation,
dependent suspension culture of T cells with cytotoxic activity.																										
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	HHAAF20	1169	IL-13 in HMC		diabetes mellitus, endocarditis, meningitis, Lyme Disease, cardiac reperfusion injury, and asthma and allergy. An additional preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease").
221	HHAAF20	1169	Activation of	Kinase assav Kinase assavs	A hiohly nreferred
221	02 1881111	1107	Activation of Natural Killer Cell ERK Signaling	for example an Elk-1 kinase assays, assay, for ERK signal	embodiment of the invention includes a method for
			Pathway.	transduction that regulate cell proliferation or differentiation are well known in the art and	stimulating natural killer cell proliferation. An alternative highly preferred embodiment
				may be used or routinely modified to assess the ability of polypeptides of the	of the invention includes a method for inhibiting natural killer cell proliferation.
				invention (including antibodies and agonists or antagonists of the invention) to promote or	highly preferred embodiment of the invention includes a method for stimulating natural
				inhibit cell proliferation, activation, and differentiation.	killer cell differentiation. An alternative highly preferred
			-	kinase activity that may be used or routinely modified to	od Ja
				activity of polypeptides of the invention (including antibodies and agonists or antagonists of	preferred indications include neoplastic diseases (e.g., as described below under

	the invention) include the	"Hyperproliferative
<del></del>	assays disclosed in Forrer et	Disorders"), blood disorders
	al., Biol Chem 379(8-9):1101-	(e.g., as described below under
	1110 (1998); Kyriakis JM,	with "Immune Activity",
	Biochem Soc Symp 64:29-48	"Cardiovascular Disorders",
	(1999); Chang and Karin,	and/or "Blood-Related
	Nature 410(6824):37-40	Disorders"), immune disorders
	(2001); and Cobb MH, Prog	(e.g., as described below under
	Biophys Mol Biol 71(3-4):479-	"Immune Activity") and
	500 (1999); the contents of	infections (e.g., as described
	each of which are herein	below under "Infectious
	incorporated by reference in its	Disease"). Preferred
	entirety. Natural killer cells	indications include blood
	that may be used according to	disorders (e.g., as described
	these assays are publicly	below under "Immune
	available (e.g., through the	Activity", "Blood-Related
	ATCC). Exemplary natural	Disorders", and/or
	killer cells that may be used	"Cardiovascular Disorders").
	according to these assays	Highly preferred indications
	include the human natural	include autoimmune diseases
	killer cell lines (for example,	(e.g., rheumatoid arthritis,
	NK-YT cells which have	systemic lupus erythematosis,
	cytolytic and cytotoxic	multiple sclerosis and/or as
	activity) or primary NK cells.	described below) and
		immunodeficiencies (e.g., as
		described below). Additional
		highly preferred indications
		include inflammation and
		inflammatory disorders.
		Highly preferred indications
		also include cancers such as,

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kidney, melanoma, prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver, urinary cancer, lymphoma and leukemias.  Other preferred indications include benign dysproliferative	disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Other highly preferred indications include,	pancytopenia, leukopenia, leukemias, Hodgkin's disease, acute lymphocytic anemia (ALL), arthritis, asthma,	AIDS, granulomatous disease, inflammatory bowel disease, sepsis, psoriasis, immune reactions to transulanted	organs and tissues, endocarditis, meningitis, Lyme Disease, and allergies.	A highly preferred embodiment of the invention includes a method for	stimulating adipocyte proliferation. An alternative highly preferred embodiment
					Kinase assay. Kinase assays, for example an Elk-1 kinase assay, for ERK signal	transduction that regulate cell proliferation or differentiation are well known in the art and
					Activation of Adipocyte ERK Signaling Pathway	
					1170	
					HHBCS39	
					222	

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	adipocyte profileration. A highly preferred embodiment	of the invention includes a	method for stimulating	adipocyte differentiation. An	alternative highly preferred	embodiment of the invention	includes a method for	inhibiting adipocyte	differentiation. A highly	preferred embodiment of the	invention includes a method	for stimulating (e.g.,	increasing) adipocyte	activation. An alternative	highly preferred embodiment	of the invention includes a	method for inhibiting the	activation of (e.g., decreasing)	and/or inactivating adipocytes.	Highly preferred indications	include endocrine disorders	(e.g., as described below under	"Endocrine Disorders").	Highly preferred indications	also include neoplastic	diseases (e.g., lipomas,	liposarcomas, and/or as	described below under	"Hyperproliferative
modified to assess the ability	or porypeptions or the invention (including antibodies	and agonists or antagonists of	the invention) to promote or	inhibit cell proliferation,	activation, and differentiation.	Exemplary assays for ERK	kinase activity that may be	used or routinely modified to	test ERK kinase-induced	activity of polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) include the	assays disclosed in Forrer et	al., Biol Chem 379(8-9):1101-	1110 (1998); Le Marchand-	Brustel Y, Exp Clin	Endocrinol Diabetes	107(2):126-132 (1999);	Kyriakis JM, Biochem Soc	Symp 64:29-48 (1999); Chang	and Karin, Nature	410(6824):37-40 (2001); and	Cobb MH, Prog Biophys Mol	Biol 71(3-4):479-500 (1999);	the contents of each of which	are herein incorporated by	reference in its entirety.	Mouse adipocyte cells that
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Disorders"), Preferred	indications include blood	disorders (e.g., hypertension,	congestive heart failure, blood	vessel blockage, heart disease,	stroke, impotence and/or as	described below under	"Immune Activity",	"Cardiovascular Disorders",	and/or "Blood-Related	Disorders"), immune disorders	(e.g., as described below under	"Immune Activity"), neural	disorders (e.g., as described	below under "Neural Activity	and Neurological Diseases"),	and infection (e.g., as	described below under	"Infectious Disease").	A highly preferred indication	is diabetes mellitus. An	additional highly preferred	indication is a complication	associated with diabetes (e.g.,	diabetic retinopathy, diabetic	nephropathy, kidney disease	(e.g., renal failure,	nephropathy and/or other	diseases and disorders as	described in the "Renal	Disorders" section below).
may be used according to these	assays are publicly available	(e.g., through the ATCC).	Exemplary mouse adipocyte	cells that may be used	according to these assays	include 3T3-L1 cells. 3T3-L1	is an adherent mouse	preadipocyte cell line that is a	continuous substrain of 3T3	fibroblast cells developed	through clonal isolation and	undergo a pre-adipocyte to	adipose-like conversion under	appropriate differentiation	conditions known in the art.															
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	diabetic neuropathy, nerve	disease and nerve damage	(e.g., due to diabetic	neuropathy), blood vessel	blockage, heart disease, stroke,	impotence (e.g., due to diabetic	neuropathy or blood vessel	blockage), seizures, mental	confusion, drowsiness,	nonketotic hyperglycemic-	hyperosmolar coma,	cardiovascular disease (e.g.,	heart disease, atherosclerosis,	microvascular disease,	hypertension, stroke, and other	diseases and disorders as	described in the	"Cardiovascular Disorders"	section below), dyslipidemia,	endocrine disorders (as	described in the "Endocrine	Disorders" section below),	neuropathy, vision impairment	(e.g., diabetic retinopathy and	blindness), ulcers and impaired	wound healing, infection (e.g.,	infectious diseases and	disorders as described in the	"Infectious Diseases" section	below (particularly of the	urinary tract and skin). An
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additional highly preferred indication is obesity and/or	complications associated with	obesity. Additional highly	preferred indications include	weight loss or alternatively,	weight gain. Additional	highly preferred indications are	complications associated with	insulin resistance.	Additional highly preferred	indications are disorders of the	musculoskeletal systems	including myopathies,	muscular dystrophy, and/or as	described herein.	Additional highly preferred	indications include,	hypertension, coronary artery	disease, dyslipidemia,	gallstones, osteoarthritis,	degenerative arthritis, eating	disorders, fibrosis, cachexia,	and kidney diseases or	disorders, Preferred	indications include neoplasms	and cancer, such as,	lymphoma, leukemia and	breast, colon, and kidney	cancer. Additional preferred
									·					14	72													

					prostate, lung, pancreatic, esophageal, stomach, brain, liver, and urinary cancer. Highly preferred indications
					include lipomas and liposarcomas. Other preferred
					indications include benign dysproliferative disorders and
					pre-neoplastic conditions, such as, for example, hyperplasia,
222	HHBCS39	1170	SEAP in HIB/CRE		metaplasia, and/or dysplasia.
222	HHBCS39	1170	TNFa in Human T- cell 2B9		
	HHEAA08	1171	Activation of	Kinase assay. Kinase assays,	A highly preferred
223			Adipocyte ERK	for example an Elk-1 kinase	embodiment of the invention
			Signaling Pathway	assay, for ERK signal	includes a method for
				transduction that regulate cell	stimulating adipocyte
				proliferation or differentiation	proliferation. An alternative
				are well known in the art and	highly preferred embodiment
				may be used or routinely	of the invention includes a
				modified to assess the ability	method for inhibiting
				of polypeptides of the	adipocyte proliferation. A
				invention (including antibodies	highly preferred embodiment
				and agonists or antagonists of	of the invention includes a
				the invention) to promote or	method for stimulating
<del></del>				inhibit cell proliferation,	adipocyte differentiation. An
				activation, and differentiation.	alternative highly preferred
				Exemplary assays for ERK	embodiment of the invention
				kinase activity that may be	includes a method for

		used or routinely modified to	inhibiting adipocyte
		test ERK kinase-induced	differentiation. A highly
		activity of polypeptides of the	dime
		invention (including antibodies	invention includes a method
-		and agonists or antagonists of	for stimulating (e.g.,
Tuley		the invention) include the	increasing) adipocyte
		assays disclosed in Forrer et	activation. An alternative
		al., Biol Chem 379(8-9):1101-	highly preferred embodiment
		1110 (1998); Le Marchand-	of the invention includes a
		Brustel Y, Exp Clin	method for inhibiting the
		Endocrinol Diabetes	activation of (e.g., decreasing)
		107(2):126-132 (1999);	and/or inactivating adipocytes.
		Kyriakis JM, Biochem Soc	Highly preferred indications
		Symp 64:29-48 (1999); Chang	include endocrine disorders
		and Karin, Nature	(e.g., as described below under
		410(6824):37-40 (2001); and	"Endocrine Disorders").
		Cobb MH, Prog Biophys Mol	Highly preferred indications
		Biol 71(3-4):479-500 (1999);	also include neoplastic
		the contents of each of which	diseases (e.g., lipomas,
		are herein incorporated by	liposarcomas, and/or as
		reference in its entirety.	described below under
		Mouse adipocyte cells that	"Hyperproliferative
		may be used according to these	Disorders"). Preferred
		assays are publicly available	indications include blood
		(e.g., through the ATCC).	disorders (e.g., hypertension,
		Exemplary mouse adipocyte	congestive heart failure, blood
		cells that may be used	vessel blockage, heart disease,
		according to these assays	stroke, impotence and/or as
		include 3T3-L1 cells. 3T3-L1	described below under
		is an adherent mouse	"Immune Activity",
	and the second s	preadipocyte cell line that is a	"Cardiovascular Disorders",

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and/on "Discal Deleted	Disorders" imming disorders	Disolders ), Infillingle disorders	(e.g., as described below under	"Immune Activity"), neural	disorders (e.g., as described	below under "Neural Activity	and Neurological Diseases"),	and infection (e.g., as	described below under	"Infectious Disease").	A highly preferred indication	is diabetes mellitus. An	additional highly preferred	indication is a complication	associated with diabetes (e.g.,	diabetic retinopathy, diabetic	nephropathy, kidney disease	(e.g., renal failure,	nephropathy and/or other	diseases and disorders as	described in the "Renal	Disorders" section below),	diabetic neuropathy, nerve	disease and nerve damage	(e.g., due to diabetic	neuropathy), blood vessel	blockage, heart disease, stroke,	impotence (e.g., due to diabetic	neuropathy or blood vessel	blockage), seizures, mental	conflicion drowcinese
continuous substanta of 3T2	fibroblast cells develoned	thereast cents developed	unrough cional isolation and	undergo a pre-adipocyte to	adipose-like conversion under	appropriate differentiation	conditions known in the art.																								41
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nonketotic hyperglycemic-	hyperosmolar coma,	cardiovascular disease (e.g.,	heart disease, atherosclerosis,	microvascular disease,	hypertension, stroke, and other	diseases and disorders as	described in the	"Cardiovascular Disorders"	section below), dyslipidemia,	endocrine disorders (as	described in the "Endocrine	Disorders" section below),	neuropathy, vision impairment	(e.g., diabetic retinopathy and	blindness), ulcers and impaired	wound healing, infection (e.g.,	infectious diseases and	disorders as described in the	"Infectious Diseases" section	below (particularly of the	urinary tract and skin). An	additional highly preferred	indication is obesity and/or	complications associated with	obesity. Additional highly	preferred indications include	weight loss or alternatively,	weight gain. Additional	highly preferred indications are	complications associated with
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		ins	insulin resistance. Additional highly preferred
		pui	indications are disorders of the
		nw	musculoskeletal systems
		inc	including myopathies,
		nm	muscular dystrophy, and/or as
		ep	described herein.
		PA	Additional highly preferred
		hui	indications include,
	,	hyl	hypertension, coronary artery
		dis	disease, dyslipidemia,
		gal	gallstones, osteoarthritis,
		gab	degenerative arthritis, eating
		dis	disorders, fibrosis, cachexia,
		and	and kidney diseases or
		dis	disorders. Preferred
		hui	indications include neoplasms
		and	and cancer, such as,
		lyn	lymphoma, leukemia and
	прина	bre	breast, colon, and kidney
		can	cancer. Additional preferred
-		hii	indications include melanoma,
		pro	prostate, lung, pancreatic,
		eso	esophageal, stomach, brain,
		live	liver, and urinary cancer.
•		Hig	Highly preferred indications
		inc	include lipomas and
		lipo	liposarcomas. Other preferred
		bui	indications include benign
		dys	dysproliferative disorders and
		nre	nre-neonlastic conditions such

as, for example, hyperplasia, metaplasia, and/or dysplasia.						
					RANTES FMAT. Assays for immunomodulatory proteins that induce chemotaxis of T cells, monocytes, and eosinophils are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mediate immunomodulation, induce chemotaxis, and/or mediate humoral or cellmediate humoral or cellmediates, such as RANTES,	and the induction of chemotactic responses in
	CD152 in Human T cells	RANTES in Human T cells	IL-5 in Th2	IL-6 in HUVEC	Production of RANTES in endothelial cells (such as human umbilical vein endothelial cells (HUVEC))	
	1171	1171	1171	1172	1172	:
	HHEAA08	HHEAA08	HHEAA08	HHEMA59	ННЕМА59	
	223	223	223	224	1479	

immune cells. Such assays	that may be used or routinely	modified to test	immunomodulatory activity of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include the assays	disclosed in Miraglia et al., J	Biomolecular Screening 4:193-	204 (1999); Rowland et al.,	"Lymphocytes: a practical	approach" Chapter 6:138-160	(2000): Cocchi et al., Science	270(5243):1811-1815 (1995);	and Robinson et al., Clin Exp	Immunol 101(3):398-407	(1995), the contents of each of	which are herein incorporated	by reference in its entirety.	Endothelial cells that may be	used according to these assays	are publicly available (e.g.,	through the ATCC).	Exemplary endothelial cells	that may be used according to	these assays include human	umbilical vein endothelial cells	(HUVEC), which are	endothelial cells which line	venous blood vessels, and are
														~																
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				involved in functions that	
				include, but are not limited to,	
				angiogenesis, vascular	
_				permeability, vascular tone,	
				and immune cell extravasation.	
	HHEMA59	1172	Activation of	Assays for the activation of	A preferred embodiment of
224			transcription	transcription through the	the invention includes a
			through serum	Serum Response Element	method for inhibiting (e.g.,
			response element in	(SRE) are well-known in the	reducing) TNF alpha
			immune cells (such	art and may be used or	production. An alternative
			as natural killer	routinely modified to assess	highly preferred embodiment
			cells).	the ability of polypeptides of	of the invention includes a
	_			the invention (including	method for stimulating (e.g.,
				antibodies and agonists or	increasing) TNF alpha
				antagonists of the invention) to	production. Preferred
				regulate serum response	indications include blood
				factors and modulate the	disorders (e.g., as described
-				expression of genes involved	below under "Immune
				in growth and upregulate the	Activity", "Blood-Related
				function of growth-related	Disorders", and/or
				genes in many cell types.	"Cardiovascular Disorders"),
				Exemplary assays for	Highly preferred indications
				transcription through the SRE	include autoimmune diseases
				that may be used or routinely	(e.g., rheumatoid arthritis,
				modified to test SRE activity	systemic lupus erythematosis,
				of the polypeptides of the	Crohn"s disease, multiple
-				invention (including antibodies	sclerosis and/or as described
				and agonists or antagonists of	below), immunodeficiencies
				the invention) include assays	(e.g., as described below),
				disclosed in Berger et al., Gene	boosting a T cell-mediated
				66:1-10 (1998); Cullen and	immune response, and

		Malm Methods in Enzymol	beteipen-lleo T e pulisted
-		216.362-368 (1992): Henthorm	immino romono Additional
		210:302-308 (1322), Heliululli	iniliume response. Additional
		et al., Proc Natl Acad Sci USA	highly preferred indications
		85:6342-6346 (1988); Benson	include inflammation and
		et al., J Immunol 153(9):3862-	inflammatory disorders, and
		3873 (1994); and Black et al.,	treating joint damage in
		Virus Genes 12(2):105-117	patients with rheumatoid
		(1997), the content of each of	arthritis. An additional highly
		which are herein incorporated	preferred indication is sepsis.
		by reference in its entirety. T	Highly preferred indications
		cells that may be used	include neoplastic diseases
		according to these assays are	(e.g., leukemia, lymphoma,
		publicly available (e.g.,	and/or as described below
		through the ATCC).	under "Hyperproliferative
		Exemplary T cells that may be	Disorders"). Additionally,
		used according to these assays	highly preferred indications
		include the NK-YT cell line,	include neoplasms and
		which is a human natural killer	cancers, such as, for example,
		cell line with cytolytic and	leukemia, lymphoma,
		cytotoxic activity.	melanoma, glioma (e.g.,
			malignant glioma), solid
			tumors, and prostate, breast,
			lung, colon, pancreatic,
			esophageal, stomach, brain,
			liver and urinary cancer. Other
			preferred indications include
			benign dysproliferative
			disorders and pre-neoplastic
			conditions, such as, for
	***		example, hyperplasia,
			metaplasia, and/or dysplasia.

				Preferred indications include
				leukopenia, thrombocytopenia,
				Hodgkin's disease, acute
				lymphocytic anemia (ALL),
				plasmacytomas, multiple
				myeloma, Burkitt's lymphoma,
				arthritis, AIDS, granulomatous
				disease, inflammatory bowel
				disease, neutropenia,
				neutrophilia, psoriasis,
				suppression of immune
				reactions to transplanted
				organs and tissues, hemophilia,
				hypercoagulation, diabetes
				mellitus, endocarditis,
				meningitis, Lyme Disease,
				cardiac reperfusion injury, and
				asthma and allergy. An
				additional preferred indication
				is infection (e.g., an infectious
				disease as described below
				under "Infectious Disease").
HHEMA/5	1173	Activation of	Assays for the activation of	Preferred indications include
		transcription	transcription through the	blood disorders (e.g., as
		through cAMP	cAMP response element are	described below under
		response element in	well-known in the art and may	"Immune Activity"; "Blood-
		immune cells (such	be used or routinely modified	Related Disorders", and/or
		as T-cells).	to assess the ability of	"Cardiovascular Disorders"),
			polypeptides of the invention	and infection (e.g., an
į			(including antibodies and	infectious disease as described

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below under "Infectious Disease"). Preferred indications include	autoimmune diseases (e.g., rheumatoid arthritis, systemic	lupus erythematosis, multiple	sclerosis and/or as described   below), immunodeficiencies	(e.g., as described below),	boosting a T cell-mediated	immune response, and	suppressing a T cell-mediated	immune response. Additional	preferred indications include	inflammation and	inflammatory disorders.	Highly preferred indications	include neoplastic diseases	(e.g., leukemia, lymphoma,	and/or as described below	under "Hyperproliferative	Disorders"). Highly preferred	indications include neoplasms	and cancers, such as, leukemia,	lymphoma (e.g., T cell	lymphoma, Burkitt's	lymphoma, non-Hodgkins	lymphoma, Hodgkin"s	disease), melanoma, and	prostate, breast, lung, colon,	pancreatic, esophageal,
agonists or antagonists of the invention) to increase cAMP, bind to CREB transcription	factor, and modulate expression of genes involved	in a wide variety of cell	functions. Exemplary assays for transcription through the	cAMP response element that	may be used or routinely	modified to test cAMP-	response element activity of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include assays	disclosed in Berger et al., Gene	66:1-10 (1998); Cullen and	Malm, Methods in Enzymol	216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA	85:6342-6346 (1988); Black et	al., Virus Genes 15(2):105-117	(1997); and Belkowski et al., J	Immunol 161(2):659-665	(1998), the contents of each of	which are herein incorporated	by reference in its entirety. T	cells that may be used	according to these assays are	publicly available (e.g.,
					-1-1-						-															
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			through the ATCC).  Exemplary human T cells that may be used according to these assays include the JURKAT	stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and
			cell line, which is a suspension culture of leukemia cells that produce IL-2 when stimulated.	pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia.
				Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, acute lymphocytic anemia
	**			(ALL), plasmacytomas, multiple myeloma, arthritis,
	W. C.			AIDS, granulomatous disease, inflammatory bowel disease,
				sepsis, neutropenia, neutrophilia, psoriasis,
				suppression of immune reactions to transplanted
	·			organs and tissues,
				diabetes mellitus, endocarditis,
	1			meningitis, Lyme Disease, and asthma and allergy.
HHEMA75	1173	SEAP in Jurkat/IL4 promoter		
HHEMA75	1173	Activation of	Assays for the activation of	Highly preferred indications
		transcription	transcription through the	include blood disorders (e.g.,
		through NFAT	Nuclear Factor of Activated T	as described below under
		response element in	cells (NFAT) response element	"Immune Activity", "Blood-

		as natural killer	may be used or routinely	"Cardiovascular Disorders")
		cells).	modified to assess the ability	Highly preferred indications
			of polypeptides of the	include autoimmune diseases
			invention (including antibodies	(e.g., rheumatoid arthritis,
			and agonists or antagonists of	systemic lupus erythematosis,
			the invention) to regulate	multiple sclerosis and/or as
			NFAT transcription factors and	described below),
			modulate expression of genes	immunodeficiencies (e.g., as
			involved in	described below), boosting a T
-			immunomodulatory functions.	cell-mediated immune
			Exemplary assays for	response, and suppressing a T
			transcription through the	cell-mediated immune
			NFAT response element that	response. Additional highly
			may be used or routinely	preferred indications include
			modified to test NFAT-	inflammation and
	-		response element activity of	inflammatory disorders. An
			polypeptides of the invention	additional highly preferred
,			(including antibodies and	indication is infection (e.g., an
			agonists or antagonists of the	infectious disease as described
			invention) include assays	below under "Infectious
			disclosed in Berger et al., Gene	Disease"). Preferred
			66:1-10 (1998); Cullen and	indications include neoplastic
			Malm, Methods in Enzymol	diseases (e.g., leukemia,
,			216:362-368 (1992); Henthorn	lymphoma, and/or as described
			et al., Proc Natl Acad Sci USA	below under
			85:6342-6346 (1988);	"Hyperproliferative
			Aramburu et al., J Exp Med	Disorders"). Preferred
			182(3):801-810 (1995); De	indications include neoplasms
			Boer et al., Int J Biochem Cell	and cancers, such as, for
			Biol 31(10):1221-1236 (1999);	example, leukemia, lymphoma,
			Fraser et al., Eur J Immunol	and prostate, breast, lung,

				29(3):838-844 (1999); and	colon, pancreatic, esophageal,
				Yeseen et al., J Biol Chem	stomach, brain, liver and
				268(19):14285-14293 (1993),	urinary cancer. Other preferred
				the contents of each of which	indications include benign
_				are herein incorporated by	dysproliferative disorders and
				reference in its entirety. NK	pre-neoplastic conditions, such
				cells that may be used	as, for example, hyperplasia,
				according to these assays are	metaplasia, and/or dysplasia.
				publicly available (e.g.,	Preferred indications also
				through the ATCC).	include anemia, pancytopenia,
<del></del>			-	Exemplary human NK cells	leukopenia, thrombocytopenia,
				that may be used according to	Hodgkin's disease, acute
				these assays include the NK-	lymphocytic anemia (ALL),
				YT cell line, which is a human	plasmacytomas, multiple
				natural killer cell line with	myeloma, Burkitt's lymphoma,
				cytolytic and cytotoxic	arthritis, AIDS, granulomatous
				activity.	disease, inflammatory bowel
_					disease, sepsis, neutropenia,
					neutrophilia, psoriasis,
					suppression of immune
					reactions to transplanted
					organs and tissues,
					hemophilia, hypercoagulation,
					diabetes mellitus, endocarditis,
					meningitis, Lyme Disease,
	THIENCARE	1173	GT 4 D :		asthma and allergy.
375	HILEIMIA/3	11/3	NEAF III		
C77			INDIO/31A10		
	HHEMA75	1173	Activation of	Assays for the activation of	Preferred indications
225			transcription	transcription through the AP1	include neoplastic diseases
	-		through AP1	response element are well-	(e.g., as described below under

	response element in	known in the art and may be	"Hyperproliferative
	immune cells (such	used or routinely modified to	Disorders"), blood disorders
	as T-cells).	assess the ability of	(e.g., as described below under
		polypeptides of the invention	"Immune Activity",
		(including antibodies and	"Cardiovascular Disorders",
		agonists or antagonists of the	and/or "Blood-Related
		invention) to modulate growth	Disorders"), and infection
		and other cell functions.	(e.g., an infectious disease as
-		Exemplary assays for	described below under
		transcription through the AP1	"Infectious Disease"). Highly
		response element that may be	preferred indications include
		used or routinely modified to	autoimmune diseases (e.g.,
		test AP1-response element	rheumatoid arthritis, systemic
		activity of polypeptides of the	lupus erythematosis, multiple
		invention (including antibodies	sclerosis and/or as described
		and agonists or antagonists of	below) and
		the invention) include assays	immunodeficiencies (e.g., as
		disclosed in Berger et al., Gene	described below). Additional
		66:1-10 (1988); Cullen and	highly preferred indications
		Malm, Methods in Enzymol	include inflammation and
		216:362-368 (1992); Henthorn	inflammatory disorders.
		et al., Proc Natl Acad Sci USA	Highly preferred indications
		85:6342-6346 (1988);	also include neoplastic
		Rellahan et al., J Biol Chem	diseases (e.g., leukemia,
		272(49):30806-30811 (1997);	lymphoma, and/or as described
		Chang et al., Mol Cell Biol	below under
		18(9):4986-4993 (1998); and	"Hyperproliferative
		Fraser et al., Eur J Immunol	Disorders"). Highly preferred
		29(3):838-844 (1999), the	indications include neoplasms
		contents of each of which are	and cancers, such as, leukemia,
		herein incorporated by	lymphoma, prostate, breast,

				reference in its entirety.	lung, colon, pancreatic,
				Human T cells that may be	esophageal, stomach, brain,
				used according to these assays	liver, and urinary cancer. Other
				are publicly available (e.g.,	preferred indications include
				through the ATCC).	benign dysproliferative
	-			Exemplary human T cells that	disorders and pre-neoplastic
				may be used according to these	conditions, such as, for
				assays include the SUPT cell	example, hyperplasia,
				line, which is an IL-2 and IL-4	metaplasia, and/or dysplasia.
				responsive suspension-culture	Preferred indications include
_				cell line.	arthritis, asthma, AIDS,
					allergy, anemia, pancytopenia,
					leukopenia, thrombocytopenia,
					Hodgkin's disease, acute
					lymphocytic anemia (ALL),
					plasmacytomas, multiple
					myeloma, Burkitt's lymphoma,
					granulomatous disease,
					inflammatory bowel disease,
					sepsis, psoriasis, suppression of
-					immune reactions to
					transplanted organs and
					tissues, endocarditis,
					meningitis, and Lyme Disease.
300	HHEMA75	1173	Activation of	Assays for the activation of	A highly preferred
C77			transcription	transcription through the CD28	embodiment of the invention
			through CD28	response element are well-	includes a method for
			response element in	known in the art and may be	stimulating T cell proliferation.
			immune cells (such	used or routinely modified to	An alternative highly preferred
			as T-cells).	assess the ability of	embodiment of the invention
				polypeptides of the invention	includes a method for

(including antibodies and	inhibiting T cell proliferation.
agonists or antagonists of the	A highly preferred
 invention) to stimulate IL-2	embodiment of the invention
 expression in T cells.	includes a method for
Exemplary assays for	activating T cells. An
transcription through the CD28	alternative highly preferred
response element that may be	embodiment of the invention
used or routinely modified to	includes a method for
 test CD28-response element	inhibiting the activation of
 activity of polypeptides of the	and/or inactivating T cells.
invention (including antibodies	A highly preferred
and agonists or antagonists of	embodiment of the invention
the invention) include assays	includes a method for
disclosed in Berger et al., Gene	stimulating (e.g., increasing)
66:1-10 (1998); Cullen and	IL-2 production. An alternative
 Malm, Methods in Enzymol	highly preferred embodiment
 216:362-368 (1992); Henthorn	of the invention includes a
 et al., Proc Natl Acad Sci USA	method for inhibiting (e.g.,
85:6342-6346 (1988);	reducing) IL-2 production.
McGuire and Iacobelli, J	Additional highly preferred
Immunol 159(3):1319-1327	indications include
(1997); Parra et al., J Immunol	inflammation and
166(4):2437-2443 (2001); and	inflammatory disorders.
Butscher et al., J Biol Chem	Highly preferred indications
3(1):552-560 (1998), the	include autoimmune diseases
contents of each of which are	(e.g., rheumatoid arthritis,
herein incorporated by	systemic lupus erythematosis,
reference in its entirety. T	multiple sclerosis and/or as
cells that may be used	described below),
according to these assays are	immunodeficiencies (e.g., as
publicly available (e.g.,	described below), boosting a T

		through the ATCC).	cell-mediated immune
		Exemplary human T cells that	response, and suppressing a T
	-	may be used according to these	cell-mediated immune
		assays include the SUPT cell	response. Highly preferred
	-,-	line, which is a suspension	indications include neoplastic
		culture of IL-2 and IL-4	diseases (e.g., melanoma, renal
		responsive T cells.	cell carcinoma, leukemia,
	<b>.</b>		lymphoma, and/or as described
	<u>.</u>		below under
 -	,,,		"Hyperproliferative
			Disorders"). Highly preferred
 -			indications include neoplasms
			and cancers, such as, for
	-		example, melanoma (e.g.,
			metastatic melanoma), renal
 -			cell carcinoma (e.g., metastatic
	•		renal cell carcinoma),
	-		leukemia, lymphoma (e.g., T
			cell lymphoma), and prostate,
 			breast, lung, colon, pancreatic,
			esophageal, stomach, brain,
			liver and urinary cancer. Other
			preferred indications include
			benign dysproliferative
			disorders and pre-neoplastic
			conditions, such as, for
	-		example, hyperplasia,
			metaplasia, and/or dysplasia.
			A highly preferred indication
			includes infection (e.g.,
			AIDS, tuberculosis, infections

associated with granulomatous disease, and osteoporosis, and/or as described below under "Infectious Disease"). A highly preferred indication is	AIDS. Additional highly preferred indications include suppression of immune reactions to transplanted organs and/or tissues, uveitis,	psoriasis, and tropical spastic paraparesis. Preferred indications include blood disorders (e.g., as described below under "Immune	Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"). Preferred indications also include anemia, pancytopenia,	leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, granulomatous	disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, hemophilia, hypercoagulation, diabetes mellitus, endocarditis,

					meningitis, Lyme Disease, asthma and allergy.
}	HHEMA75	1173	Activation of	Assays for the activation of	Highly preferred indications
225	-		transcription	transcription through the	include neoplastic diseases
			through GAS	Gamma Interferon Activation	(e.g., leukemia, lymphoma,
			response element in	Site (GAS) response element	and/or as described below
			immune cells (such	are well-known in the art and	under "Hyperproliferative
			as T-cells).	may be used or routinely	Disorders"). Highly preferred
				modified to assess the ability	indications include neoplasms
				of polypeptides of the	and cancers, such as, for
				invention (including antibodies	example, leukemia, lymphoma
				and agonists or antagonists of	(e.g., T cell lymphoma,
				the invention) to regulate	Burkitt's lymphoma, non-
				STAT transcription factors and	Hodgkins lymphoma,
				modulate gene expression	Hodgkin"s disease),
				involved in a wide variety of	melanoma, and prostate,
				cell functions. Exemplary	breast, lung, colon, pancreatic,
				assays for transcription	esophageal, stomach, brain,
				through the GAS response	liver and urinary cancer. Other
				element that may be used or	preferred indications include
				routinely modified to test	benign dysproliferative
				GAS-response element activity	disorders and pre-neoplastic
				of polypeptides of the	conditions, such as, for
				invention (including antibodies	example, hyperplasia,
				and agonists or antagonists of	metaplasia, and/or dysplasia.
				the invention) include assays	Preferred indications include
				disclosed in Berger et al., Gene	autoimmune diseases (e.g.,
				66:1-10 (1998); Cullen and	rheumatoid arthritis, systemic
				Malm, Methods in Enzymol	lupus erythematosis, multiple
	-			216:362-368 (1992); Henthorn	sclerosis and/or as described
!				et al., Proc Natl Acad Sci USA	below), immunodeficiencies

(e.g., as described below),	boosting a 1 cell-mediated	immune response, and	suppressing a T cell-mediated	immune response. Additional	preferred indications include	inflammation and	inflammatory disorders.	Highly preferred indications	include blood disorders (e.g.,	as described below under	"Immune Activity", "Blood-	Related Disorders", and/or	"Cardiovascular Disorders"),	and infection (e.g., viral	infections, tuberculosis,	infections associated with	chronic granulomatosus	disease and malignant	osteoporosis, and/or an	infectious disease as described	below under "Infectious	Disease"). An additional	preferred indication is	idiopathic pulmonary fibrosis.	Preferred indications include	anemia, pancytopenia,	leukopenia, thrombocytopenia,	acute lymphocytic anemia	(ALL), plasmacytomas,	multiple myeloma, arthritis,
85:6342-6346 (1988);	Matikainen et al., Blood	93(6):1980-1991 (1999); and	Henttinen et al., J Immunol	155(10):4582-4587 (1995), the	contents of each of which are	herein incorporated by	reference in its entirety.	Exemplary human T cells,	such as the SUPT cell line, that	may be used according to these	assays are publicly available	(e.g., through the ATCC).																		
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he die ass	Assays for the activation of transcription through the Nuclear Factor of Activated T cells (NFAT) response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate NFAT transcription factors and modulate expression of genes involved in immunomodulatory functions. Exemplary assays for transcription through the NFAT response element that may be used or routinely
	HHEMA75 1173 Activation of transcription through NFAT response eleme immune cells (as T-cells).

response element activity of	inflammatory disorders. An
polypeptides of the invention	additional highly preferred
(including antibodies and	indication is infection (e.g., an
agonists or antagonists of the	infectious disease as described
 invention) include assays	below under "Infectious
disclosed in Berger et al., Gene	Disease"). Preferred
66:1-10 (1998); Cullen and	indications include neoplastic
Malm, Methods in Enzymol	diseases (e.g., leukemia,
216:362-368 (1992); Henthorn	lymphoma, and/or as described
et al., Proc Natl Acad Sci USA	below under
 85:6342-6346 (1988); Serfling	"Hyperproliferative
et al., Biochim Biophys Acta	Disorders"). Preferred
1498(1):1-18 (2000); De Boer	indications include neoplasms
et al., Int J Biochem Cell Biol	and cancers, such as, for
31(10):1221-1236 (1999);	example, leukemia, lymphoma,
 Fraser et al., Eur J Immunol	and prostate, breast, lung,
29(3):838-844 (1999); and	colon, pancreatic, esophageal,
 Yeseen et al., J Biol Chem	stomach, brain, liver and
268(19):14285-14293 (1993),	urinary cancer. Other preferred
the contents of each of which	indications include benign
are herein incorporated by	dysproliferative disorders and
reference in its entirety. T	pre-neoplastic conditions, such
 cells that may be used	as, for example, hyperplasia,
according to these assays are	metaplasia, and/or dysplasia.
publicly available (e.g.,	Preferred indications also
through the ATCC).	include anemia, pancytopenia,
Exemplary human T cells that	leukopenia, thrombocytopenia,
 may be used according to these	Hodgkin's disease, acute
 assays include the SUPT cell	lymphocytic anemia (ALL),
line, which is a suspension	plasmacytomas, multiple
culture of IL-2 and IL-4	myeloma, Burkitt's lymphoma,

				responsive T cells.	arthritis. AIDS. granulomatous
<del></del>					disease, inflammatory bowel
					disease, sepsis, neutropenia,
					neutrophilia, psoriasis,
_					suppression of immune
					reactions to transplanted
					organs and tissues,
					hemophilia, hypercoagulation,
					diabetes mellitus, endocarditis,
					meningitis, Lyme Disease,
					asthma and allergy.
300	HHEMA75	1173	Activation of	Assays for the activation of	Highly preferred indications
577			transcription	transcription through the	include inflammation and
			through NFKB	NFKB response element are	inflammatory disorders.
			response element in	well-known in the art and may	Highly preferred indications
			immune cells (such	be used or routinely modified	include blood disorders (e.g.,
10.0			as T-cells).	to assess the ability of	as described below under
				polypeptides of the invention	"Immune Activity", "Blood-
				(including antibodies and	Related Disorders", and/or
				agonists or antagonists of the	"Cardiovascular Disorders").
	-1u-2			invention) to regulate NFKB	Highly preferred indications
41				transcription factors and	include autoimmune diseases
				modulate expression of	(e.g., rheumatoid arthritis,
				immunomodulatory genes.	systemic lupus erythematosis,
				Exemplary assays for	multiple sclerosis and/or as
				transcription through the	described below), and
			-	NFKB response element that	immunodeficiencies (e.g., as
				may be used or rountinely	described below). An
		_		modified to test NFKB-	additional highly preferred
				response element activity of	indication is infection (e.g.,
				polypeptides of the invention	AIDS, and/or an infectious

		(including antibodies and	disease as described below
		agonists or antagonists of the	under "Infectious Disease").
		invention) include assays	Highly preferred indications
		disclosed in Berger et al., Gene	include neoplastic diseases
		66:1-10 (1998); Cullen and	(e.g., melanoma, leukemia,
		Malm, Methods in Enzymol	lymphoma, and/or as described
		216:362-368 (1992); Henthorn	below under
-		et al., Proc Natl Acad Sci USA	"Hyperproliferative
		85:6342-6346 (1988); Black et	Disorders"). Highly preferred
		al., Virus Gnes 15(2):105-117	indications include neoplasms
		(1997); and Fraser et al.,	and cancers, such
		29(3):838-844 (1999), the	as,melanoma, renal cell
		contents of each of which are	carcinoma, leukemia,
		herein incorporated by	lymphoma, and prostate,
		reference in its entirety. T	breast, lung, colon, pancreatic,
		cells that may be used	esophageal, stomach, brain,
		according to these assays are	liver and urinary cancer. Other
		publicly available (e.g.,	preferred indications include
		through the ATCC).	benign dysproliferative
		Exemplary human T cells that	disorders and pre-neoplastic
		may be used according to these	conditions, such as, for
		assays include the SUPT cell	example, hyperplasia,
		line, which is a suspension	metaplasia, and/or dysplasia.
		culture of IL-2 and IL-4	Preferred indications also
		responsive T cells.	include anemia, pancytopenia,
			leukopenia, thrombocytopenia,
			Hodgkin's disease, acute
			lymphocytic anemia (ALL),
			plasmacytomas, multiple
			myeloma, Burkitt's lymphoma,
	1, 10, 11		arthritis, AIDS,

					granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, suppression of immune reactions to transplanted organs, asthma and alleroy.
526	HHEMM74	1174	Activation of transcription through cAMP response element in immune cells (such as T-cells).	Assays for the activation of transcription through the cAMP response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to increase cAMP and regulate CREB transcription factors, and modulate expression of genes involved in a wide variety of cell functions. Exemplary	Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"), and infection (e.g., an infectious disease as described below under "Infectious Disease"). Preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below), immunodeficiencies
				through the cAMP response element that may be used or routinely modified to test cAMP-response element activity of polypeptides of the	(e.g., as described below), boosting a T cell-mediated immune response, and suppressing a T cell-mediated immune response. Additional

			invention (including antibodies and agonists or antagonists of	preferred indications include inflammation and
			the invention) include assays	inflammatory disorders.
			disclosed in Berger et al., Gene	Highly preferred indications
			66:1-10 (1998); Cullen and	include neoplastic diseases
	•		Malm, Methods in Enzymol	(e.g., leukemia, lymphoma,
			216:362-368 (1992); Henthorn	and/or as described below
			et al., Proc Natl Acad Sci USA	under "Hyperproliferative
			85:6342-6346 (1988); Black et	Disorders"). Highly preferred
			al., Virus Genes 15(2):105-117	indications include neoplasms
			(1997); and Belkowski et al., J	and cancers, such as, for
			Immunol 161(2):659-665	example, leukemia, lymphoma
			(1998), the contents of each of	(e.g., T cell lymphoma,
			which are herein incorporated	Burkitt's lymphoma, non-
			by reference in its entirety. T	Hodgkins lymphoma,
	•		cells that may be used	Hodgkin's disease),
			according to these assays are	melanoma, and prostate,
			publicly available (e.g.,	breast, lung, colon, pancreatic,
-	141.		through the ATCC).	esophageal, stomach, brain,
			Exemplary mouse T cells that	liver and urinary cancer. Other
			may be used according to these	preferred indications include
			assays include the CTLL cell	benign dysproliferative
			line, which is a suspension	disorders and pre-neoplastic
			culture of IL-2 dependent	conditions, such as, for
			cytotoxic T cells.	example, hyperplasia,
				metaplasia, and/or dysplasia.
				Preferred indications include
				anemia, pancytopenia,
				leukopenia, thrombocytopenia,
				acute lymphocytic anemia
				(ALL), plasmacytomas,

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multiple myeloma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, and asthma and allergy.	A highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing) IL-6 production. An alternative highly preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) IL-6 production. A highly preferred indication is the stimulation or enhancement of mucosal immunity. Highly preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"), and infection (e.g., as
·	IL-6 FMAT. IL-6 is produced by T cells and has strong effects on B cells. IL-6 participates in IL-4 induced lgE production and increases lgA production (IgA plays a role in mucosal immunity). IL-6 induces cytotoxic T cells. Deregulated expression of IL-6 has been linked to autoimmune disease, plasmacytomas, myelomas, and chronic hyperproliferative diseases. Assays for immunomodulatory and differentiation factor proteins produced by a large variety of cells where the expression level is strongly regulated by cytokines, growth
	Production of IL-6
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